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SEARCH REQ

Requester's Full Name: [illegible] Date: 05.30.08

Art Unit: 1625 Phone Number: 2-6202 Serial Number: 10/599,497

Location: (Bldg/Room) REM 4D54 Mailbox #: 1625 Results Format Preferred (circle): PAPER DISK

MS

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: Methods for the preparation of [illegible]

Inventors (please provide full names): [illegible]

Earliest Priority Date: [illegible]

Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known.

For Sequence Searches Only: Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

```
=> file registry
FILE 'REGISTRY' ENTERED AT 10:38:28 ON 03 JUN 2008
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STRUCTURE FILE UPDATES: 2 JUN 2008 HIGHEST RN 1024742-83-3
DICTIONARY FILE UPDATES: 2 JUN 2008 HIGHEST RN 1024742-83-3

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TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> file zcaplus
FILE 'ZCAPLUS' ENTERED AT 10:38:32 ON 03 JUN 2008
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FILE COVERS 1907 - 3 Jun 2008 VOL 148 ISS 23
FILE LAST UPDATED: 2 Jun 2008 (20080602/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.
'OBI' IS DEFAULT SEARCH FIELD FOR 'ZCAPLUS' FILE

=> d stat que L21
L3 17 SEA FILE=REGISTRY ABB=ON PLU=ON (104321-62-2/BI OR 124-41-4/BI OR 156928-09-5/BI OR 22323-80-4/BI OR 501921-30-8/BI OR 6674-22-2/BI OR 67-63-0/BI OR 75-52-5/BI OR 75-65-0/BI OR 75-75-2/BI OR 75-85-4/BI OR 80-70-6/BI OR 865-34-9/BI OR 866594-60-7/BI OR 866594-61-8/BI OR 867-13-0/BI OR 94697-68-4/BI)
L4 84397 SEA FILE=REGISTRY ABB=ON PLU=ON 2 OC4/ESS
L5 4 SEA FILE=REGISTRY ABB=ON PLU=ON L3 AND L4
L6 1642 SEA FILE=REGISTRY ABB=ON PLU=ON C6H10O3/MF
L7 22 SEA FILE=REGISTRY ABB=ON PLU=ON L6 AND L4
L10 20 SEA FILE=REGISTRY ABB=ON PLU=ON "FURO(2,3-B)FURAN-3-OL, HEXAHYDRO-"?/CN
L12 7 SEA FILE=REGISTRY ABB=ON PLU=ON L7 AND L10
L14 43 SEA FILE=ZCAPLUS ABB=ON PLU=ON L12

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L16             3 SEA FILE=REGISTRY ABB=ON  PLU=ON  L5 NOT L12
L20             5 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L16
L21             3 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L14 AND L20


=> d stat que L25
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                  I OR 156928-09-5/BI OR 22323-80-4/BI OR 501921-30-8/BI OR
                  6674-22-2/BI OR 67-63-0/BI OR 75-52-5/BI OR 75-65-0/BI OR
                  75-75-2/BI OR 75-85-4/BI OR 80-70-6/BI OR 865-34-9/BI OR
                  866594-60-7/BI OR 866594-61-8/BI OR 867-13-0/BI OR 94697-68-4/B
                  I)
L4          84397 SEA FILE=REGISTRY ABB=ON  PLU=ON  2 OC4/ESS
L5              4 SEA FILE=REGISTRY ABB=ON  PLU=ON  L3 AND L4
L6           1642 SEA FILE=REGISTRY ABB=ON  PLU=ON  C6H10O3/MF
L7             22 SEA FILE=REGISTRY ABB=ON  PLU=ON  L6 AND L4
L10            20 SEA FILE=REGISTRY ABB=ON  PLU=ON  "FURO(2,3-B)FURAN-3-OL,
                  HEXAHYDRO-"?/CN
L12             7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L7 AND L10
L14            43 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L12
L16             3 SEA FILE=REGISTRY ABB=ON  PLU=ON  L5 NOT L12
L20             5 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L16
L21             3 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L14 AND L20
L22            32 SEA FILE=REGISTRY ABB=ON  PLU=ON  (104321-62-2/BI OR 156928-09-
                  5/BI OR 22323-80-4/BI OR 867-13-0/BI OR 94697-68-4/BI OR
                  108-59-8/BI OR 204390-79-4/BI OR 501921-30-8/BI OR 866594-60-7/
                  BI OR 124-41-4/BI OR 144114-21-6/BI OR 252873-00-0/BI OR
                  501921-23-9/BI OR 501921-24-0/BI OR 501921-25-1/BI OR 501921-26
                  -2/BI OR 501921-27-3/BI OR 501921-28-4/BI OR 501921-29-5/BI OR
                  501921-31-9/BI OR 501921-32-0/BI OR 6674-22-2/BI OR 67-63-0/BI
                  OR 75-52-5/BI OR 75-65-0/BI OR 75-75-2/BI OR 75-85-4/BI OR
                  80-70-6/BI OR 865-34-9/BI OR 866594-61-8/BI OR 874290-09-2/BI
                  OR 874290-10-5/BI)
L23       1933411 SEA FILE=REGISTRY ABB=ON  PLU=ON  ?NITRO?/CNS
L24             4 SEA FILE=REGISTRY ABB=ON  PLU=ON  L22 AND L23
L25             2 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L24 AND L21


=> d stat que L39
L4          84397 SEA FILE=REGISTRY ABB=ON  PLU=ON  2 OC4/ESS
L6           1642 SEA FILE=REGISTRY ABB=ON  PLU=ON  C6H10O3/MF
L7             22 SEA FILE=REGISTRY ABB=ON  PLU=ON  L6 AND L4
L10            20 SEA FILE=REGISTRY ABB=ON  PLU=ON  "FURO(2,3-B)FURAN-3-OL,
                  HEXAHYDRO-"?/CN
L12             7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L7 AND L10
L14            43 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L12
L23       1933411 SEA FILE=REGISTRY ABB=ON  PLU=ON  ?NITRO?/CNS
L33               TRANSFER  PLU=ON  L14 1- RN :    3468 TERMS
L34          3468 SEA FILE=REGISTRY ABB=ON  PLU=ON  L33
L35           102 SEA FILE=REGISTRY ABB=ON  PLU=ON  L34 AND L23
L36            50 SEA FILE=REGISTRY ABB=ON  PLU=ON  L35 AND ?NITROPHENYL?/CNS
L37            52 SEA FILE=REGISTRY ABB=ON  PLU=ON  L35 NOT L36
L38             4 SEA FILE=REGISTRY ABB=ON  PLU=ON  L37 AND ?NITROMETHYL?/CNS
L39             2 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L38 AND L14


=> => file registry
FILE 'REGISTRY' ENTERED AT 10:47:45 ON 03 JUN 2008
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STRUCTURE FILE UPDATES: 2 JUN 2008 HIGHEST RN 1024742-83-3
DICTIONARY FILE UPDATES: 2 JUN 2008 HIGHEST RN 1024742-83-3

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Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> file zcaplus
FILE 'ZCAPLUS' ENTERED AT 10:47:54 ON 03 JUN 2008
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FILE COVERS 1907 - 3 Jun 2008 VOL 148 ISS 23
FILE LAST UPDATED: 2 Jun 2008 (20080602/ED)

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'OBI' IS DEFAULT SEARCH FIELD FOR 'ZCAPLUS' FILE

=> d stat que L61
L50 52 SEA FILE=ZCAPLUS ABB=ON PLU=ON QUAEDFLIEG P?/AU
L51 33 SEA FILE=ZCAPLUS ABB=ON PLU=ON KESTELEYN B?/AU
L52 15 SEA FILE=ZCAPLUS ABB=ON PLU=ON VIJN R?/AU
L53 3 SEA FILE=ZCAPLUS ABB=ON PLU=ON LIEBREGTS C?/AU
L54 46 SEA FILE=ZCAPLUS ABB=ON PLU=ON KOOISTRA J?/AU
L55 10 SEA FILE=ZCAPLUS ABB=ON PLU=ON LOMMEN F?/AU
L56 3 SEA FILE=ZCAPLUS ABB=ON PLU=ON L50 AND (L51 OR L52 OR L53 OR L54 OR L55)
L57 2 SEA FILE=ZCAPLUS ABB=ON PLU=ON L51 AND (L52 OR L53 OR L54 OR L55)
L58 3 SEA FILE=ZCAPLUS ABB=ON PLU=ON L52 AND (L53 OR L54 OR L55)

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L59             2 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L53 AND (L54 OR L55)
L60             1 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L54 AND L55
L61             3 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  (L56 OR L57 OR L58 OR L59 OR
                  L60)


=> d stat que L63
L4          84397 SEA FILE=REGISTRY ABB=ON  PLU=ON  2 OC4/ESS
L50            52 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  QUAEDFLIEG P?/AU
L51            33 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  KESTELEYN B?/AU
L52            15 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  VIJN R?/AU
L53             3 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  LIEBREGTS C?/AU
L54            46 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  KOOISTRA J?/AU
L55            10 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  LOMMEN F?/AU
L62         63018 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L4
L63             4 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  (L50 OR L51 OR L52 OR L53 OR
                  L54 OR L55) AND L62


=> s L61 or L63
L72             5 L61 OR L63

=> file casreact
FILE 'CASREACT' ENTERED AT 10:48:15 ON 03 JUN 2008
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FILE CONTENT:1840 - 31 May 2008 VOL 148 ISS 23

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************************************************************
*                                                          *
*     CASREACT now has more than 13.8 million reactions    *
*                                                          *
************************************************************

Some CASREACT records are derived from the ZIC/VINITI database (1974-1999)
provided by InfoChem, INPI data prior to 1986, and Biotransformations
database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance
identification.

=> d stat que L71
L3             17 SEA FILE=REGISTRY ABB=ON  PLU=ON  (104321-62-2/BI OR 124-41-4/B
                  I OR 156928-09-5/BI OR 22323-80-4/BI OR 501921-30-8/BI OR
                  6674-22-2/BI OR 67-63-0/BI OR 75-52-5/BI OR 75-65-0/BI OR
                  75-75-2/BI OR 75-85-4/BI OR 80-70-6/BI OR 865-34-9/BI OR
                  866594-60-7/BI OR 866594-61-8/BI OR 867-13-0/BI OR 94697-68-4/B
                  I)
L4          84397 SEA FILE=REGISTRY ABB=ON  PLU=ON  2 OC4/ESS
L5              4 SEA FILE=REGISTRY ABB=ON  PLU=ON  L3 AND L4
L6           1642 SEA FILE=REGISTRY ABB=ON  PLU=ON  C6H10O3/MF
L7             22 SEA FILE=REGISTRY ABB=ON  PLU=ON  L6 AND L4
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L10          20 SEA FILE=REGISTRY ABB=ON  PLU=ON  "FURO(2,3-B)FURAN-3-OL,
                HEXAHYDRO-"?/CN
L12           7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L7 AND L10
L16           3 SEA FILE=REGISTRY ABB=ON  PLU=ON  L5 NOT L12
L40          18 SEA FILE=CASREACT ABB=ON  PLU=ON  L12
L41           3 SEA FILE=CASREACT ABB=ON  PLU=ON  L16
L42           1 SEA FILE=CASREACT ABB=ON  PLU=ON  L40 (L) L41
L68           3 SEA FILE=CASREACT ABB=ON  PLU=ON  ("138:238003"/AN OR "143:3870
                12"/AN OR "144:170908"/AN OR "148:379603"/AN OR "2003:221694"/A
                N OR "2005:1103784"/AN OR "2005:1257726"/AN OR "2008:381168"/AN
                )
L71           3 SEA FILE=CASREACT ABB=ON  PLU=ON  L68 AND (L40 OR L41 OR L42)


=> d ibib abs hitind hitstr L72 tot; d ibib abs hit L71 tot
YOU HAVE REQUESTED DATA FROM FILE 'ZCAPLUS' - CONTINUE? (Y)/N:y



L72  ANSWER 1 OF 5  ZCAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2008:381168  ZCAPLUS  Full-text
DOCUMENT NUMBER:          148:379603
TITLE:                    Process for preparation of hexahydrofuro[2,3-b]furan-3-
                          ol derivatives
INVENTOR(S):              Quaedflieg, Peter Jan Leonard Mario; Sereinig,
                          Natascha; Alsters, Paulus Lambertus; Straatman,
                          Henricus Martinus Maria Gerardus; Hanbauer, Martin
                          Helmut Friedrich; Ronde, Niek Johannes
PATENT ASSIGNEE(S):       DSM IP Assets B.V., Neth.
SOURCE:                   PCT Int. Appl., 34pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
     WO 2008034598        A1    20080327    WO 2007-EP8148         20070919
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA,
             CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI,
             GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG,
             KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME,
             MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL,
             PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN,
             TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW,
             GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.:                       EP 2006-19537       A  20060919
OTHER SOURCE(S):          CASREACT 148:379603; MARPAT 148:379603
AB    The present invention relates to a method for producing enantiomerically and
      diastereomerically enriched hexahydrofuro[2,3-b]furan-3-ol compds., which
      comprises aldol addition of two suitable O-protected hydroxyaldehydes and
      subsequent removal of the protecting groups and (optionally simultaneous)
      cyclization of the resulting aldol compound and subsequent isolation of the
      desired compds.  The resulting composition can be further diastereomerically
```

enriched through the intermittent acylation of the compound and further optionally using a stereoselective hydrolytic enzyme.

CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 7

IT 162119-35-9P
RL: IMF (Industrial manufacture); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of hexahydrofuro[2,3-b]furan-3-ol derivs.)

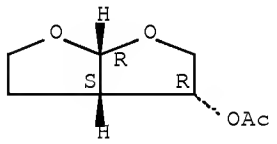
IT 4435-55-6P 5371-49-3P 6564-95-0P 18621-75-5P 20267-19-0P 35435-68-8P 72117-30-7P 72157-18-7P 87184-81-4P 87184-99-4P 156928-09-5P 305856-92-2P 1015081-28-3P 1015081-29-4P 1015081-30-7P 1015081-31-8P 1015081-32-9P 1015081-34-1P 1015081-35-2P 1015081-36-3P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of hexahydrofuro[2,3-b]furan-3-ol derivs.)

IT 156928-10-8P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of hexahydrofuro[2,3-b]furan-3-ol derivs.)

IT 162119-35-9P
RL: IMF (Industrial manufacture); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of hexahydrofuro[2,3-b]furan-3-ol derivs.)

RN 162119-35-9 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, 3-acetate, (3R,3aS,6aR)- (CA INDEX NAME)

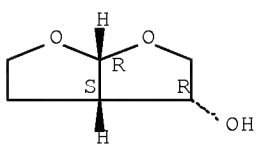
Absolute stereochemistry. Rotation (-).



IT 156928-09-5P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of hexahydrofuro[2,3-b]furan-3-ol derivs.)

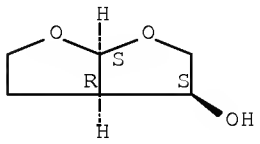
RN 156928-09-5 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



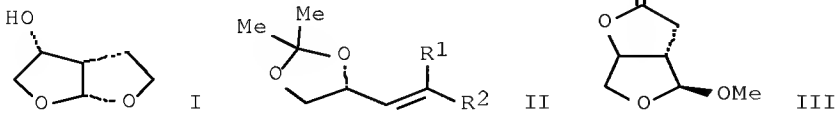
IT 156928-10-8P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of hexahydrofuro[2,3-b]furan-3-ol derivs.)
RN 156928-10-8 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3S,3aR,6aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L72 ANSWER 2 OF 5 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1257726 ZCAPLUS Full-text
DOCUMENT NUMBER: 144:170908
TITLE: Stereoselective and Efficient Synthesis of (3R,3aS,6aR)-Hexahydrofuro[2,3-b]furan-3-ol
AUTHOR(S): Quaedflieg, Peter J. L. M.; Kesteleyn, Bart P. R.; Wigerinck, Piet B. T. P.; Goyvaerts, Nicolaas M. F.; Vijn, Robert Jan; Liebregts, Constantinus S. M.; Kooistra, Jaap H. M. H.; Cusan, Claudia
CORPORATE SOURCE: LS-ASCD, DSM Pharma Chemicals, Geleen, 6160 MD, Neth.
SOURCE: Organic Letters (2005), 7(26), 5917-5920
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 144:170908
GI



AB Two short and efficient synthesis routes have been developed for (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-ol I, a key building block of the investigational HIV protease inhibitor TMC114, using (S)-2,3-O- isopropylideneglyceraldehyde as the source of chirality. Both routes are based on a diastereoselective Michael addition of nitromethane to α,β-unsatd. esters II (R1 = R2 = MeO2C; R1 = H, R2 = EtO2C), which gave predominantly the syn congeners, followed by a Nef oxidation and cyclization to afford lactone acetal III, which was reduced and cyclized to give I.
CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))

IT 22323-80-4P 104321-62-2P 204390-79-4P 866594-60-7P
874290-09-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(asym. synthesis of hexahydrofuro[2,3-b]furan-3-ol)

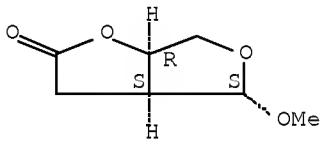
IT 156928-09-5P 874290-10-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(asym. synthesis of hexahydrofuro[2,3-b]furan-3-ol)

IT 866594-60-7P 874290-09-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(asym. synthesis of hexahydrofuro[2,3-b]furan-3-ol)

RN 866594-60-7 ZCAPLUS

CN Furo[3,4-b]furan-2(3H)-one, tetrahydro-4-methoxy-, (3aS,4S,6aR)- (CA INDEX NAME)

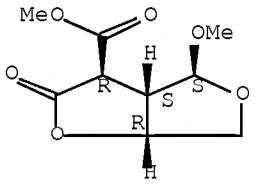
Absolute stereochemistry. Rotation (+).



RN 874290-09-2 ZCAPLUS

CN Furo[3,4-b]furan-3-carboxylic acid, hexahydro-4-methoxy-2-oxo-, methyl ester, (3R,3aS,4S,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

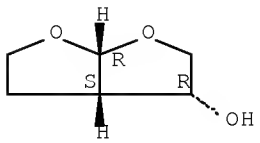


IT 156928-09-5P 874290-10-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(asym. synthesis of hexahydrofuro[2,3-b]furan-3-ol)

RN 156928-09-5 ZCAPLUS

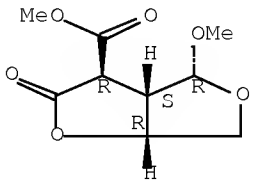
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 874290-10-5 ZCAPLUS
CN Furo[3,4-b]furan-3-carboxylic acid, hexahydro-4-methoxy-2-oxo-, methyl ester, (3R,3aS,4R,6aR)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L72 ANSWER 3 OF 5 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1103784 ZCAPLUS Full-text
DOCUMENT NUMBER: 143:387012
TITLE: Methods for the preparation of (3R,3aS,6aR) hexahydro-furo[2,3-b]furan-3-ol
INVENTOR(S): Quaedflieg, Peter Jan Leonard Mario; Kesteleyn, Bart Rudolf Romanie; Vijn, Robert Jan; Liebregts, Constantinus Simon Maria; Kooistra, Jacob Hermanus Matheus Hero; Lommen, Franciscus Alphons Marie
PATENT ASSIGNEE(S): Tibotec Pharmaceuticals Ltd., Ire.
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005095410	A1	20051013	WO 2005-EP51452	20050331
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005229435	A1	20051013	AU 2005-229435	20050331
CA 2559959	A1	20051013	CA 2005-2559959	20050331
EP 1732931	A1	20061220	EP 2005-729507	20050331
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
CN 1938316	A	20070328	CN 2005-80010400	20050331
BR 2005009514	A	20070911	BR 2005-9514	20050331

JP 2007530638	T	20071101	JP 2007-505559	20050331
IN 2006DN05301	A	20070803	IN 2006-DN5301	20060913
MX 2006PA11281	A	20061207	MX 2006-PA11281	20060929
US 20070208184	A1	20070906	US 2006-599497	20060929
NO 2006004977	A	20061031	NO 2006-4977	20061031

PRIORITY APPLN. INFO.: EP 2004-101336 A 20040331
WO 2005-EP51452 W 20050331

OTHER SOURCE(S): CASREACT 143:387012; MARPAT 143:387012

AB The present invention relates to methods for the preparation of diastereomerically pure (3R,3aS,6aR) hexahydro-furo[2,3-b]furan-3-ol (I) as well as a novel intermediate, (3aR,4S,6aS) 4-methoxy-tetrahydro- furo[3,4-b]furan-2-one (II) for use in said methods. More in particular the invention relates to a stereoselective method for the preparation of diastereomerically pure I, as well as methods for the crystallization of II and for the epimerization of (3aR,4R,6aS) 4-methoxy-tetrahydro-furo[3,4-b]- furan-2-one to II.

IC ICM C07D493-04
ICS C07D307-20; C07H015-04

CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))

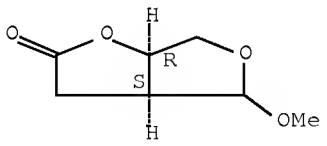
IT 22323-80-4P 104321-62-2P 501921-30-8P 866594-61-8P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(stereoselective preparation of hexahydrofuro[2,3-b]furanol utilizing a Michael addition and a Nef reaction and chiral starting materials)

IT 156928-09-5P 866594-60-7P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(stereoselective preparation of hexahydrofuro[2,3-b]furanol utilizing a Michael addition and a Nef reaction and chiral starting materials)

IT 501921-30-8P 866594-61-8P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(stereoselective preparation of hexahydrofuro[2,3-b]furanol utilizing a Michael addition and a Nef reaction and chiral starting materials)

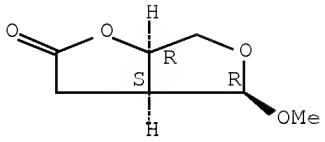
RN 501921-30-8 ZCAPLUS
CN Furo[3,4-b]furan-2(3H)-one, tetrahydro-4-methoxy-, (3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry.



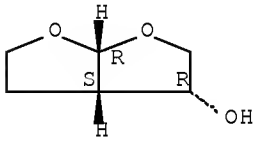
RN 866594-61-8 ZCAPLUS
CN Furo[3,4-b]furan-2(3H)-one, tetrahydro-4-methoxy-, (3aS,4R,6aR)- (CA INDEX NAME)

Absolute stereochemistry.



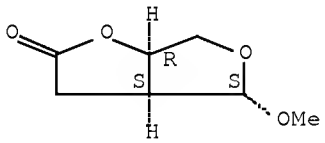
IT 156928-09-5P 866594-60-7P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(stereoselective preparation of hexahydrofuro[2,3-b]furanol utilizing a Michael addition and a Nef reaction and chiral starting materials)
RN 156928-09-5 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 866594-60-7 ZCAPLUS
CN Furo[3,4-b]furan-2(3H)-one, tetrahydro-4-methoxy-, (3aS,4S,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L72 ANSWER 4 OF 5 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:371247 ZCAPLUS Full-text
DOCUMENT NUMBER: 142:430488
TITLE: Process for the preparation of (S)-glyceraldehyde acetonide from L-ascorbic acid via oxidative bond cleavage and removal of excess H2O2 by catalase
INVENTOR(S): Quaedflieg, Peter Jan Leonard Mario; Lommen, Franciscus Alphons Marie; Vijn, Robert Jan; Boxtel Van Dannieel, Adrianus Franciscus Jacobus
PATENT ASSIGNEE(S): DSM Ip Assets B.V., Neth.
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005037819	A1	20050428	WO 2004-EP11343	20041007
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2541491	A1	20050428	CA 2004-2541491	20041007
EP 1673364	A1	20060628	EP 2004-790256	20041007
EP 1673364	B1	20070822		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1863787	A	20061115	CN 2004-80029141	20041007
JP 2007507461	T	20070329	JP 2006-530134	20041007
AT 370940	T	20070915	AT 2004-790256	20041007
ES 2290770	T3	20080216	ES 2004-790256	20041007
IN 2006DN01923	A	20070810	IN 2006-DN1923	20060407
US 20070073068	A1	20070329	US 2006-574693	20060706
US 7361775	B2	20080422		

PRIORITY APPLN. INFO.: EP 2003-78130 A 20031007
WO 2004-EP11343 W 20041007

OTHER SOURCE(S): CASREACT 142:430488

AB The invention relates to a process for the preparation of (S)-glyceraldehyde acetonide in aqueous solution from 3,4-O-isopropylidene-L-threonic acid or a salt thereof in aqueous solution, and hypochlorite in aqueous solution wherein the aqueous hypochlorite solution has a pH > 7.5 and wherein during addition of at least 0.1 molar equivalents of hypochlorite based on the amount of 3,4-O-isopropylidene-L-threonic acid, an acid solution is not simultaneously added. The invention also relates to a process according to the invention, wherein 3,4-O-isopropylidene-L-threonic acid or a salt thereof is prepared from 5,6-O-isopropylidene-L-ascorbic acid or a salt thereof in the presence of H2O2 and a base in a manner known per se, wherein excess H2O2 is optionally removed by catalase. The invention also relates to a process according to the invention, wherein 5,6-O-isopropylidene-L- ascorbic acid or a salt thereof is prepared by reacting L-ascorbic acid or a salt thereof with an acetonide forming agent, preferably in the presence of an acid catalyst.

IC ICM C07D317-26
CC 33-2 (Carbohydrates)
Section cross-reference(s): 7, 9
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L72 ANSWER 5 OF 5 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:221694 ZCAPLUS Full-text
DOCUMENT NUMBER: 138:238003
TITLE: Process for the preparation of hexahydro-furo[2,3-b]furan-3-ol via stereoselective intramolecular cyclization reaction as HIV-protease inhibitors
INVENTOR(S): Kesteleyn, Bart Rudolf Romanie; Surleraux, Dominique

Louis Nestor Ghislain
PATENT ASSIGNEE(S): Tibotec Pharmaceuticals Ltd., Ire.
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003022853	A1	20030320	WO 2002-EP10062	20020906
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2459168	A1	20030320	CA 2002-2459168	20020906
AU 2002333809	A1	20030324	AU 2002-333809	20020906
AU 2002333809	B2	20080228		
BR 2002012341	A	20040727	BR 2002-12341	20020906
EP 1448567	A1	20040825	EP 2002-797968	20020906
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
SI 21463	A	20041031	SI 2002-20026	20020906
CN 1553915	A	20041208	CN 2002-817639	20020906
JP 2005502707	T	20050127	JP 2003-526927	20020906
HU 2004002140	A2	20050228	HU 2004-2140	20020906
HU 2004002140	A3	20070529		
NZ 531641	A	20050826	NZ 2002-531641	20020906
AP 1758	A	20070831	AP 2004-2981	20020906
CN 101172980	A	20080507	CN 2007-10186668	20020906
IN 2004DN00329	A	20050401	IN 2004-DN329	20040212
ZA 2004001501	A	20050524	ZA 2004-1501	20040224
US 20040249175	A1	20041209	US 2004-489059	20040309
US 7126015	B2	20061024		
MX 2004PA02247	A	20050907	MX 2004-PA2247	20040309
NO 2004001434	A	20040610	NO 2004-1434	20040406

PRIORITY APPLN. INFO.:	EP 2001-203416	A	20010910
	CN 2002-817639	A3	20020906
	WO 2002-EP10062	W	20020906

OTHER SOURCE(S): MARPAT 138:238003

AB The present invention relates to a method for the preparation of hexahydro-furo[2,3-b]furan-3-ol via stereoselective intramol. cyclization reaction as HIV-protease inhibitor (no data) as well as novel intermediates for use in said method. More in particular the invention relates to a stereoselective method for the preparation of hexahydro-furo[2,3- b]furan-3-ol, and to a method amenable to industrial scaling up.

IC ICM C07D493-04
ICS C07D493-04; C07D307-00; C07D307-00
CC 27-7 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 7
IT 156928-09-5P 252673-00-0P
RL: IMF (Industrial manufacture); PREP (Preparation)
(Process for the preparation of hexahydro-furo[2,3-b]furan-3-ol via

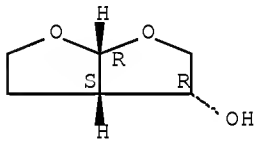
stereoselective intramol. cyclization reaction as HIV-protease inhibitors)

IT 104321-62-2P 204390-79-4P 501921-23-9P 501921-24-0P
501921-25-1P 501921-26-2P 501921-27-3P 501921-28-4P
501921-29-5P 501921-30-8P 501921-31-9P
501921-32-0P
RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(Process for the preparation of hexahydro-furo[2,3-b]furan-3-ol via stereoselective intramol. cyclization reaction as HIV-protease inhibitors)

IT 156928-09-5P 252873-00-0P
RL: IMF (Industrial manufacture); PREP (Preparation)
(Process for the preparation of hexahydro-furo[2,3-b]furan-3-ol via stereoselective intramol. cyclization reaction as HIV-protease inhibitors)

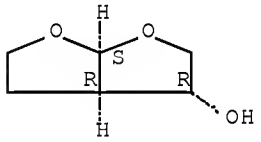
RN 156928-09-5 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 252873-00-0 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aR,6aS)- (CA INDEX NAME)

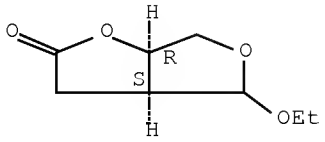
Absolute stereochemistry.



IT 501921-25-1P 501921-29-5P 501921-30-8P
501921-31-9P
RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(Process for the preparation of hexahydro-furo[2,3-b]furan-3-ol via stereoselective intramol. cyclization reaction as HIV-protease inhibitors)

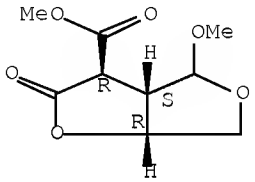
RN 501921-25-1 ZCAPLUS
CN Furo[3,4-b]furan-2(3H)-one, 4-ethoxytetrahydro-, (3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry.



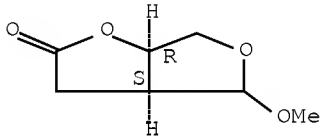
RN 501921-29-5 ZCAPLUS
CN Furo[3,4-b]furan-3-carboxylic acid, hexahydro-4-methoxy-2-oxo-, methyl ester, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry.



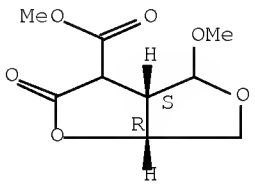
RN 501921-30-8 ZCAPLUS
CN Furo[3,4-b]furan-2(3H)-one, tetrahydro-4-methoxy-, (3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry.



RN 501921-31-9 ZCAPLUS
CN Furo[3,4-b]furan-3-carboxylic acid, hexahydro-4-methoxy-2-oxo-, methyl ester, (3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L71 ANSWER 1 OF 3 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 148:379603 CASREACT Full-text
TITLE: Process for preparation of hexahydrofuro[2,3-b]furan-3-ol derivatives
INVENTOR(S): Quaedflieg, Peter Jan Leonard Mario; Sereinig, Natascha; Alsters, Paulus Lambertus; Straatman, Henricus Martinus Maria Gerardus; Hanbauer, Martin Helmut Friedrich; Ronde, Niek Johannes
PATENT ASSIGNEE(S): DSM IP Assets B.V., Neth.
SOURCE: PCT Int. Appl., 34pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008034598	A1	20080327	WO 2007-EP8148	20070919

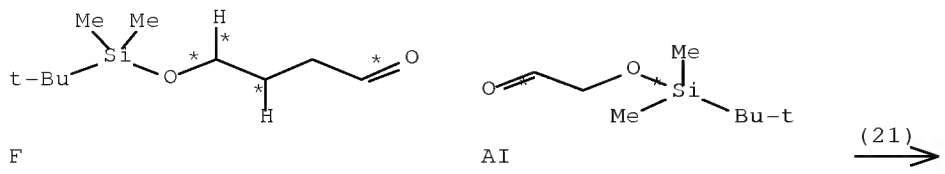
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: EP 2006-19537 20060919
OTHER SOURCE(S): MARPAT 148:379603

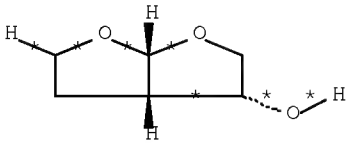
AB The present invention relates to a method for producing enantiomerically and diastereomerically enriched hexahydrofuro[2,3-b]furan-3-ol compds., which comprises aldol addition of two suitable O-protected hydroxyaldehydes and subsequent removal of the protecting groups and (optionally simultaneous) cyclization of the resulting aldol compound and subsequent isolation of the desired compds. The resulting composition can be further diastereomerically enriched through the intermittent acylation of the compound and further optionally using a stereoselective hydrolytic enzyme.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(21) OF 80 ...F + AI ===> AR...



F AI



AR
YIELD 73%

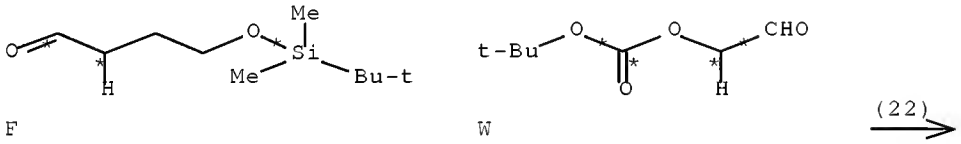
RX(21) RCT F 87184-81-4, AI 102191-92-4

STAGE(1)
CAT 147-85-3 (S)-Proline
SOL 109-99-9 THF
CON 45 hours, 4 deg C

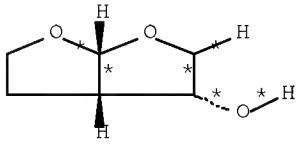
STAGE(2)
RGT AS 7647-01-0 HCl
SOL 7732-18-5 Water
CON 20 hours, 2 - 4 deg C

PRO AR 156928-09-5
NTE stereoselective

RX(22) OF 80 ...F + W ===> AR...



F W (22)



AR
YIELD 63%

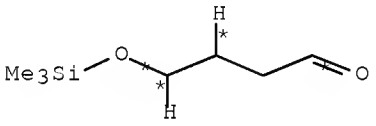
RX(22) RCT F 87184-81-4, W 1015081-35-2

STAGE(1)
CAT 147-85-3 (S)-Proline
SOL 109-99-9 THF
CON 84 hours, 4 deg C

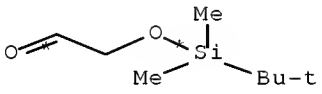
STAGE(2)
RGT AS 7647-01-0 HCl
SOL 7732-18-5 Water
CON 44 hours, 20 deg C

PRO AR 156928-09-5
NTE stereoselective

RX(23) OF 80 ...K + AI ===> AR...

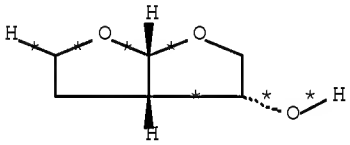


K



AI

(23)



AR
YIELD 63%

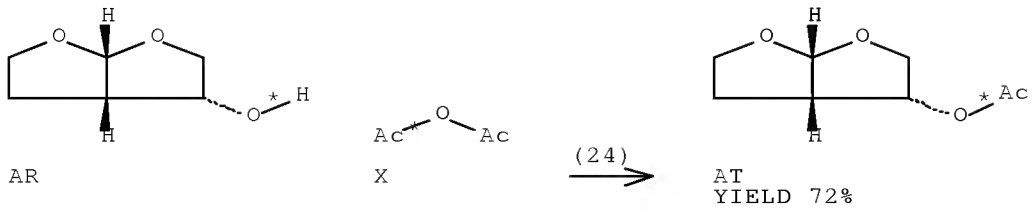
RX(23) RCT K 72157-18-7, AI 102191-92-4

STAGE(1)
CAT 147-85-3 (S)-Proline
SOL 109-99-9 THF
CON 84 hours, 4 deg C

STAGE(2)
RGT AS 7647-01-0 HCl
SOL 7732-18-5 Water
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 18 hours, 4 deg C

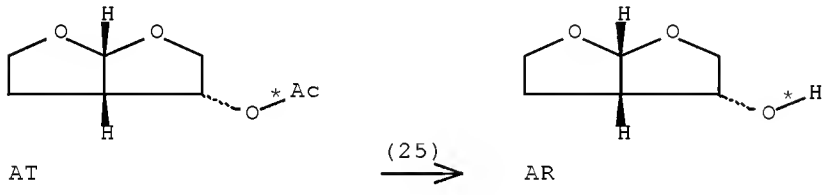
PRO AR 156928-09-5
NTE stereoselective

RX(24) OF 80 ...AR + X ===> AT



RX(24) RCT AR 156928-09-5, X 108-24-7
RGT D 121-44-8 Et3N
PRO AT 162119-35-9
CAT 1122-58-3 4-DMAP
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 3 hours, 20 deg C

RX(25) OF 80 AT ===> AR



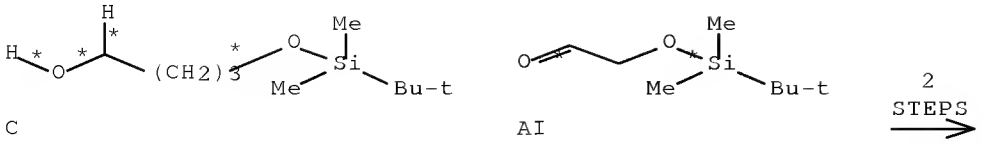
RX(25) RCT AT 162119-35-9

STAGE(1)
CAT 9001-62-1 Lipase
SOL 7732-18-5 Water
CON 24 hours, 35 deg C, pH 7

STAGE(2)
RGT AU 584-08-7 K2CO3
SOL 67-56-1 MeOH
CON room temperature

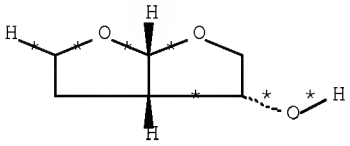
PRO AR 156928-09-5
NTE stage 1 stereoselective, enzymic, biotransformation, buffered solution

RX(31) OF 80 COMPOSED OF RX(2), RX(21)
RX(31) C + AI ===> AR



C AI

2 STEPS



AR
YIELD 73%

RX(2) RCT C 87184-99-4
RGT G 26412-87-3 Pyridine-SO3 (1:1), D 121-44-8 Et3N
PRO F 87184-81-4
SOL 108-88-3 PhMe, 67-68-5 DMSO
CON SUBSTAGE(1) 1 hour, 0 - 10 deg C
SUBSTAGE(2) 0.5 hours, 0 - 10 deg C

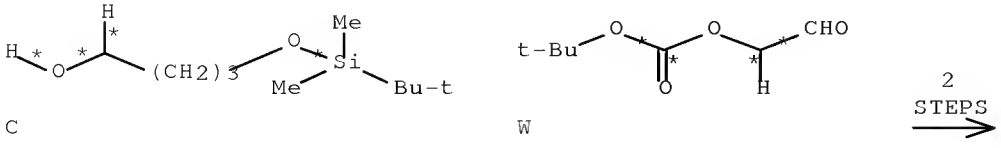
RX(21) RCT F 87184-81-4, AI 102191-92-4

STAGE(1)
CAT 147-85-3 (S)-Proline
SOL 109-99-9 THF
CON 45 hours, 4 deg C

STAGE(2)
RGT AS 7647-01-0 HCl
SOL 7732-18-5 Water
CON 20 hours, 2 - 4 deg C

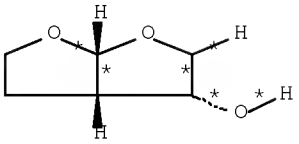
PRO AR 156928-09-5
NTE stereoselective

RX(32) OF 80 COMPOSED OF RX(2), RX(22)
RX(32) C + W ===> AR



C W

2 STEPS



AR
YIELD 63%

RX(2) RCT C 87184-99-4
RGT G 26412-87-3 Pyridine-SO3 (1:1), D 121-44-8 Et3N
PRO F 87184-81-4
SOL 108-88-3 PhMe, 67-68-5 DMSO
CON SUBSTAGE(1) 1 hour, 0 - 10 deg C
SUBSTAGE(2) 0.5 hours, 0 - 10 deg C

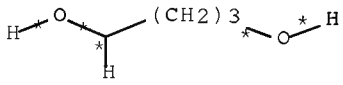
RX(22) RCT F 87184-81-4, W 1015081-35-2

STAGE(1)
CAT 147-85-3 (S)-Proline
SOL 109-99-9 THF
CON 84 hours, 4 deg C

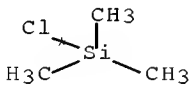
STAGE(2)
RGT AS 7647-01-0 HCl
SOL 7732-18-5 Water
CON 44 hours, 20 deg C

PRO AR 156928-09-5
NTE stereoselective

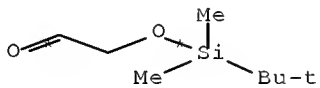
RX(34) OF 80 COMPOSED OF RX(3), RX(23)
RX(34) A + J + AI ===> AR



A

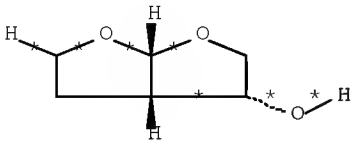


J



AI

2
STEPS



AR
YIELD 63%

RX(3) RCT A 110-63-4, J 75-77-4

STAGE(1)
RGT D 121-44-8 Et3N
CON 2 hours, room temperature

STAGE(2)
RGT G 26412-87-3 Pyridine-SO3 (1:1), D 121-44-8 Et3N
SOL 67-68-5 DMSO
CON SUBSTAGE(1) 0.5 hours, 0 - 5 deg C
SUBSTAGE(2) 4 hours, room temperature

PRO K 72157-18-7

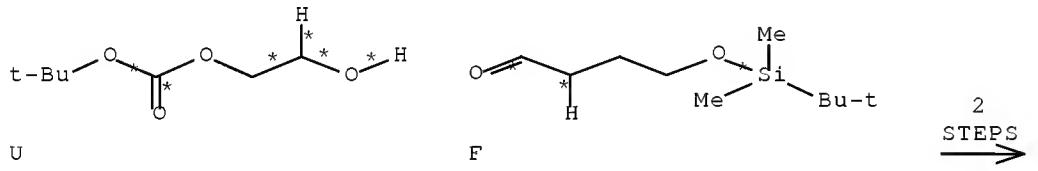
RX(23) RCT K 72157-18-7, AI 102191-92-4

STAGE(1)
CAT 147-85-3 (S)-Proline
SOL 109-99-9 THF
CON 84 hours, 4 deg C

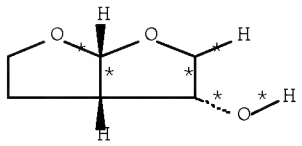
STAGE(2)
RGT AS 7647-01-0 HCl
SOL 7732-18-5 Water
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 18 hours, 4 deg C

PRO AR 156928-09-5
NTE stereoselective

RX(41) OF 80 COMPOSED OF RX(9), RX(22)
RX(41) U + F ===> AR



U F



AR
YIELD 63%

RX(9) RCT U 305856-92-2

RGT G 26412-87-3 Pyridine-SO3 (1:1), D 121-44-8 Et3N
PRO W 1015081-35-2
SOL 75-09-2 CH2Cl2, 67-68-5 DMSO
CON SUBSTAGE(1) 20 minutes, 0 - 10 deg C
SUBSTAGE(2) 1.5 hours, 0 - 10 deg C

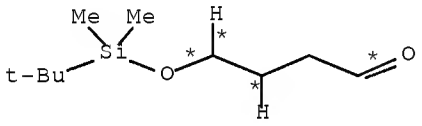
RX(22) RCT F 87184-81-4, W 1015081-35-2

STAGE(1)
CAT 147-85-3 (S)-Proline
SOL 109-99-9 THF
CON 84 hours, 4 deg C

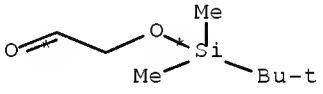
STAGE(2)
RGT AS 7647-01-0 HCl
SOL 7732-18-5 Water
CON 44 hours, 20 deg C

PRO AR 156928-09-5
NTE stereoselective

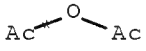
RX(44) OF 80 COMPOSED OF RX(21), RX(24)
RX(44) F + AI + X ===> AT



F

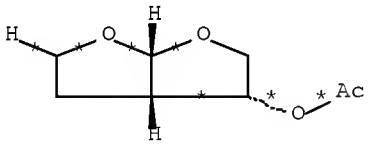


AI



X

2
STEPS



AT
YIELD 72%

RX(21) RCT F 87184-81-4, AI 102191-92-4

STAGE(1)
CAT 147-85-3 (S)-Proline
SOL 109-99-9 THF
CON 45 hours, 4 deg C

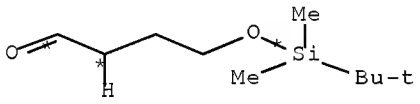
STAGE(2)
RGT AS 7647-01-0 HCl
SOL 7732-18-5 Water

CON 20 hours, 2 - 4 deg C

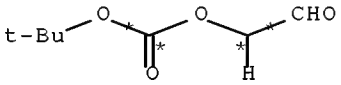
PRO AR 156928-09-5
NTE stereoselective

RX(24) RCT AR 156928-09-5, X 108-24-7
RGT D 121-44-8 Et3N
PRO AT 162119-35-9
CAT 1122-58-3 4-DMAP
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 3 hours, 20 deg C

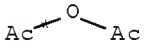
RX(45) OF 80 COMPOSED OF RX(22), RX(24)
RX(45) F + W + X ===> AT



F

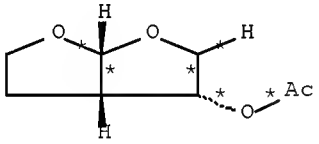


W



X

2 STEPS



AT
YIELD 72%

RX(22) RCT F 87184-81-4, W 1015081-35-2

STAGE(1)
CAT 147-85-3 (S)-Proline
SOL 109-99-9 THF
CON 84 hours, 4 deg C

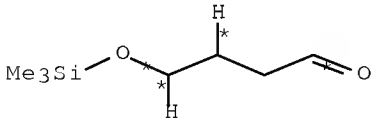
STAGE(2)
RGT AS 7647-01-0 HCl
SOL 7732-18-5 Water
CON 44 hours, 20 deg C

PRO AR 156928-09-5
NTE stereoselective

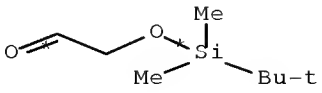
RX(24) RCT AR 156928-09-5, X 108-24-7
RGT D 121-44-8 Et3N
PRO AT 162119-35-9
CAT 1122-58-3 4-DMAP

SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 3 hours, 20 deg C

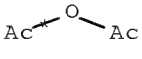
RX(46) OF 80 COMPOSED OF RX(23), RX(24)
RX(46) K + AI + X ===> AT



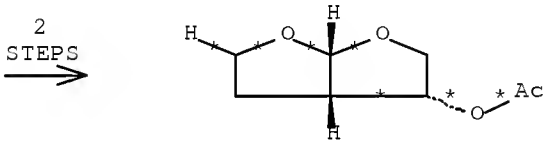
K



AI



X



AT
YIELD 72%

RX(23) RCT K 72157-18-7, AI 102191-92-4

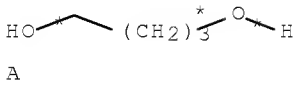
STAGE(1)
CAT 147-85-3 (S)-Proline
SOL 109-99-9 THF
CON 84 hours, 4 deg C

STAGE(2)
RGT AS 7647-01-0 HCl
SOL 7732-18-5 Water
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 18 hours, 4 deg C

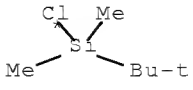
PRO AR 156928-09-5
NTE stereoselective

RX(24) RCT AR 156928-09-5, X 108-24-7
RGT D 121-44-8 Et3N
PRO AT 162119-35-9
CAT 1122-58-3 4-DMAP
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 3 hours, 20 deg C

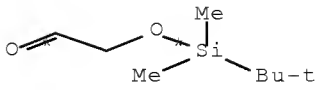
RX(51) OF 80 COMPOSED OF RX(1), RX(2), RX(21)
RX(51) A + B + AI ===> AR



A

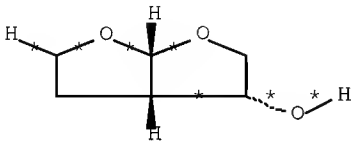


B



AI

3 STEPS



AR
YIELD 73%

RX(1) RCT A 110-63-4, B 18162-48-6
RGT D 121-44-8 Et3N
PRO C 87184-99-4
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 45 minutes, room temperature
SUBSTAGE(2) 1 hour, room temperature

RX(2) RCT C 87184-99-4
RGT G 26412-87-3 Pyridine-SO3 (1:1), D 121-44-8 Et3N
PRO F 87184-81-4
SOL 108-88-3 PhMe, 67-68-5 DMSO
CON SUBSTAGE(1) 1 hour, 0 - 10 deg C
SUBSTAGE(2) 0.5 hours, 0 - 10 deg C

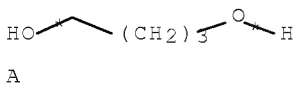
RX(21) RCT F 87184-81-4, AI 102191-92-4

STAGE(1)
CAT 147-85-3 (S)-Proline
SOL 109-99-9 THF
CON 45 hours, 4 deg C

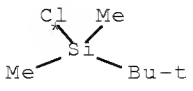
STAGE(2)
RGT AS 7647-01-0 HCl
SOL 7732-18-5 Water
CON 20 hours, 2 - 4 deg C

PRO AR 156928-09-5
NTE stereoselective

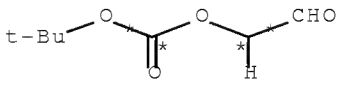
RX(52) OF 80 COMPOSED OF RX(1), RX(2), RX(22)
RX(52) A + B + W ===> AR



A

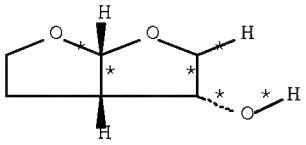


B



W

3 STEPS



AR
YIELD 63%

RX(1) RCT A 110-63-4, B 18162-48-6
RGT D 121-44-8 Et3N
PRO C 87184-99-4
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 45 minutes, room temperature
SUBSTAGE(2) 1 hour, room temperature

RX(2) RCT C 87184-99-4
RGT G 26412-87-3 Pyridine-SO3 (1:1), D 121-44-8 Et3N
PRO F 87184-81-4
SOL 108-88-3 PhMe, 67-68-5 DMSO
CON SUBSTAGE(1) 1 hour, 0 - 10 deg C
SUBSTAGE(2) 0.5 hours, 0 - 10 deg C

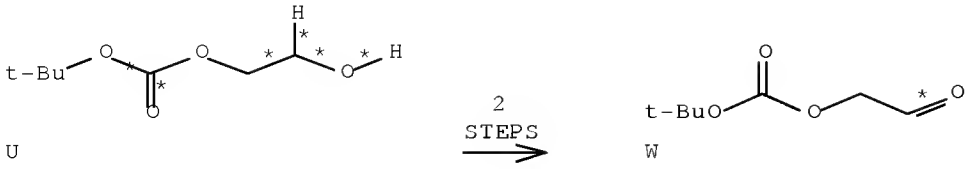
RX(22) RCT F 87184-81-4, W 1015081-35-2

STAGE(1)
CAT 147-85-3 (S)-Proline
SOL 109-99-9 THF
CON 84 hours, 4 deg C

STAGE(2)
RGT AS 7647-01-0 HCl
SOL 7732-18-5 Water
CON 44 hours, 20 deg C

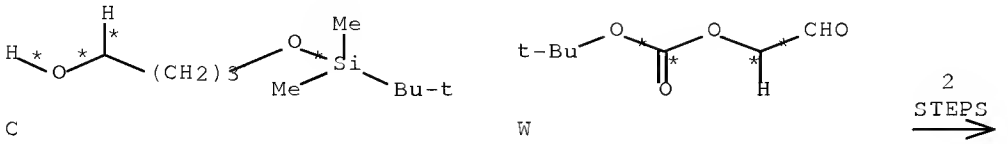
PRO AR 156928-09-5
NTE stereoselective

RX(55) OF 80 COMPOSED OF REACTION SEQUENCE RX(9), RX(22)
AND REACTION SEQUENCE RX(2), RX(22)
...U ===> W...
...C + W ===> AR

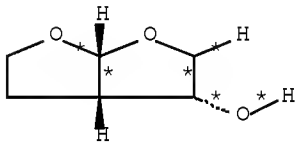


U W

START NEXT REACTION SEQUENCE



C W



AR
YIELD 63%

RX(9) RCT U 305856-92-2
RGT G 26412-87-3 Pyridine-SO3 (1:1), D 121-44-8 Et3N
PRO W 1015081-35-2
SOL 75-09-2 CH2Cl2, 67-68-5 DMSO
CON SUBSTAGE(1) 20 minutes, 0 - 10 deg C
SUBSTAGE(2) 1.5 hours, 0 - 10 deg C

RX(2) RCT C 87184-99-4
RGT G 26412-87-3 Pyridine-SO3 (1:1), D 121-44-8 Et3N
PRO F 87184-81-4
SOL 108-88-3 PhMe, 67-68-5 DMSO
CON SUBSTAGE(1) 1 hour, 0 - 10 deg C
SUBSTAGE(2) 0.5 hours, 0 - 10 deg C

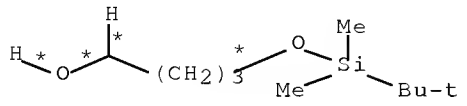
RX(22) RCT F 87184-81-4, W 1015081-35-2

STAGE(1)
CAT 147-85-3 (S)-Proline
SOL 109-99-9 THF
CON 84 hours, 4 deg C

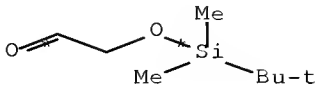
STAGE(2)
RGT AS 7647-01-0 HCl
SOL 7732-18-5 Water
CON 44 hours, 20 deg C

PRO AR 156928-09-5
NTE stereoselective

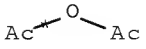
RX(56) OF 80 COMPOSED OF RX(2), RX(21), RX(24)
RX(56) C + AI + X ===> AT



C

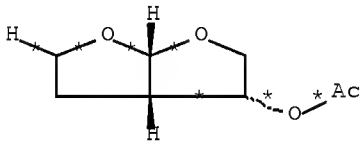


AI



X

3
STEPS



AT
YIELD 72%

RX(2) RCT C 87184-99-4
RGT G 26412-87-3 Pyridine-SO3 (1:1), D 121-44-8 Et3N
PRO F 87184-81-4
SOL 108-88-3 PhMe, 67-68-5 DMSO
CON SUBSTAGE(1) 1 hour, 0 - 10 deg C
SUBSTAGE(2) 0.5 hours, 0 - 10 deg C

RX(21) RCT F 87184-81-4, AI 102191-92-4

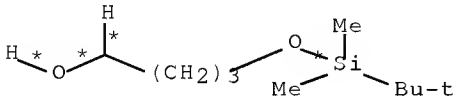
STAGE(1)
CAT 147-85-3 (S)-Proline
SOL 109-99-9 THF
CON 45 hours, 4 deg C

STAGE(2)
RGT AS 7647-01-0 HCl
SOL 7732-18-5 Water
CON 20 hours, 2 - 4 deg C

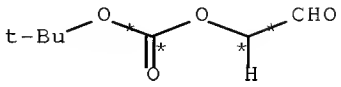
PRO AR 156928-09-5
NTE stereoselective

RX(24) RCT AR 156928-09-5, X 108-24-7
RGT D 121-44-8 Et3N
PRO AT 162119-35-9
CAT 1122-58-3 4-DMAP
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 3 hours, 20 deg C

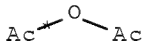
RX(57) OF 80 COMPOSED OF RX(2), RX(22), RX(24)
RX(57) C + W + X ===> AT



C

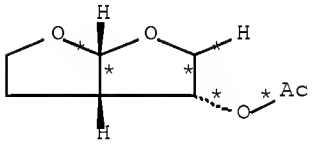


W



X

3
STEPS



AT
YIELD 72%

RX(2) RCT C 87184-99-4
RGT G 26412-87-3 Pyridine-SO3 (1:1), D 121-44-8 Et3N
PRO F 87184-81-4
SOL 108-88-3 PhMe, 67-68-5 DMSO
CON SUBSTAGE(1) 1 hour, 0 - 10 deg C
SUBSTAGE(2) 0.5 hours, 0 - 10 deg C

RX(22) RCT F 87184-81-4, W 1015081-35-2

STAGE(1)
CAT 147-85-3 (S)-Proline
SOL 109-99-9 THF
CON 84 hours, 4 deg C

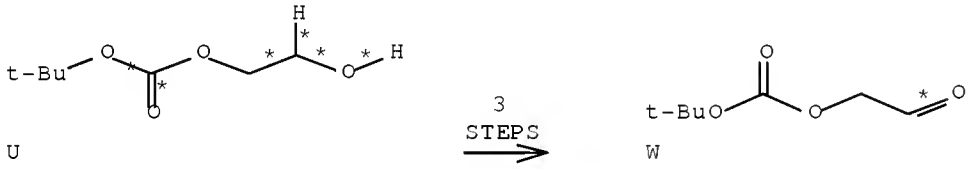
STAGE(2)
RGT AS 7647-01-0 HCl

SOL 7732-18-5 Water
CON 44 hours, 20 deg C

PRO AR 156928-09-5
NTE stereoselective

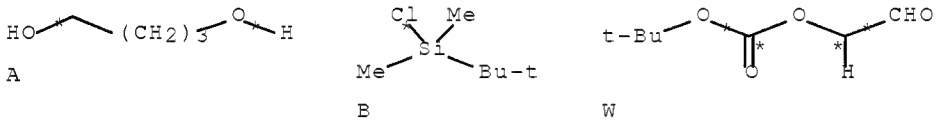
RX(24) RCT AR 156928-09-5, X 108-24-7
RGT D 121-44-8 Et3N
PRO AT 162119-35-9
CAT 1122-58-3 4-DMAP
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 3 hours, 20 deg C

RX(60) OF 80 COMPOSED OF REACTION SEQUENCE RX(9), RX(22)
AND REACTION SEQUENCE RX(1), RX(2), RX(22)
...U ===> W...
...A + B + W ===> AR

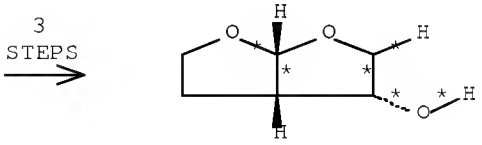


U W

START NEXT REACTION SEQUENCE



A B W



AR
YIELD 63%

RX(9) RCT U 305856-92-2
RGT G 26412-87-3 Pyridine-SO3 (1:1), D 121-44-8 Et3N
PRO W 1015081-35-2
SOL 75-09-2 CH2Cl2, 67-68-5 DMSO
CON SUBSTAGE(1) 20 minutes, 0 - 10 deg C
SUBSTAGE(2) 1.5 hours, 0 - 10 deg C

RX(1) RCT A 110-63-4, B 18162-48-6
RGT D 121-44-8 Et3N
PRO C 87184-99-4
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 45 minutes, room temperature
SUBSTAGE(2) 1 hour, room temperature

RX(2) RCT C 87184-99-4
RGT G 26412-87-3 Pyridine-SO3 (1:1), D 121-44-8 Et3N
PRO F 87184-81-4
SOL 108-88-3 PhMe, 67-68-5 DMSO
CON SUBSTAGE(1) 1 hour, 0 - 10 deg C
SUBSTAGE(2) 0.5 hours, 0 - 10 deg C

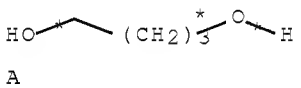
RX(22) RCT F 87184-81-4, W 1015081-35-2

STAGE(1)
CAT 147-85-3 (S)-Proline
SOL 109-99-9 THF
CON 84 hours, 4 deg C

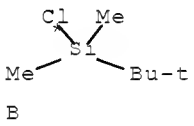
STAGE(2)
RGT AS 7647-01-0 HCl
SOL 7732-18-5 Water
CON 44 hours, 20 deg C

PRO AR 156928-09-5
NTE stereoselective

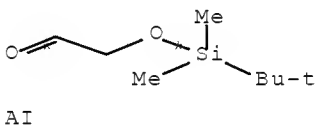
RX(61) OF 80 COMPOSED OF RX(1), RX(2), RX(21), RX(24)
RX(61) A + B + AI + X ===> AT



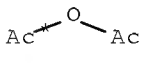
A



B

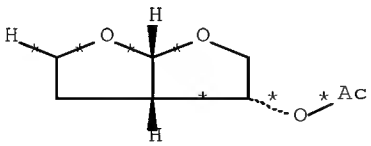


AI



X

4
STEPS



AT
YIELD 72%

RX(1) RCT A 110-63-4, B 18162-48-6
RGT D 121-44-8 Et3N
PRO C 87184-99-4
SOL 75-09-2 CH2Cl2

CON SUBSTAGE(1) 45 minutes, room temperature
SUBSTAGE(2) 1 hour, room temperature

RX(2) RCT C 87184-99-4
RGT G 26412-87-3 Pyridine-SO3 (1:1), D 121-44-8 Et3N
PRO F 87184-81-4
SOL 108-88-3 PhMe, 67-68-5 DMSO
CON SUBSTAGE(1) 1 hour, 0 - 10 deg C
SUBSTAGE(2) 0.5 hours, 0 - 10 deg C

RX(21) RCT F 87184-81-4, AI 102191-92-4

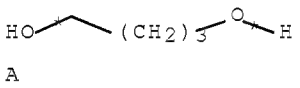
STAGE(1)
CAT 147-85-3 (S)-Proline
SOL 109-99-9 THF
CON 45 hours, 4 deg C

STAGE(2)
RGT AS 7647-01-0 HCl
SOL 7732-18-5 Water
CON 20 hours, 2 - 4 deg C

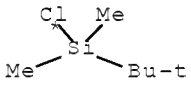
PRO AR 156928-09-5
NTE stereoselective

RX(24) RCT AR 156928-09-5, X 108-24-7
RGT D 121-44-8 Et3N
PRO AT 162119-35-9
CAT 1122-58-3 4-DMAP
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 3 hours, 20 deg C

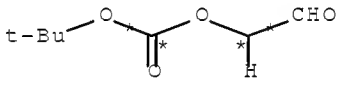
RX(62) OF 80 COMPOSED OF RX(1), RX(2), RX(22), RX(24)
RX(62) A + B + W + X ===> AT



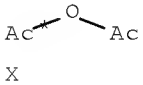
A



B

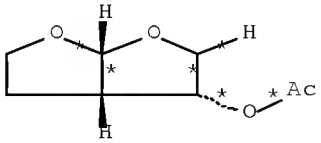


W



X

4
STEPS



AT
YIELD 72%

RX(1) RCT A 110-63-4, B 18162-48-6

RGT D 121-44-8 Et3N
PRO C 87184-99-4
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 45 minutes, room temperature
SUBSTAGE(2) 1 hour, room temperature

RX(2) RCT C 87184-99-4
RGT G 26412-87-3 Pyridine-SO3 (1:1), D 121-44-8 Et3N
PRO F 87184-81-4
SOL 108-88-3 PhMe, 67-68-5 DMSO
CON SUBSTAGE(1) 1 hour, 0 - 10 deg C
SUBSTAGE(2) 0.5 hours, 0 - 10 deg C

RX(22) RCT F 87184-81-4, W 1015081-35-2

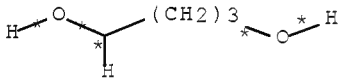
STAGE(1)
CAT 147-85-3 (S)-Proline
SOL 109-99-9 THF
CON 84 hours, 4 deg C

STAGE(2)
RGT AS 7647-01-0 HCl
SOL 7732-18-5 Water
CON 44 hours, 20 deg C

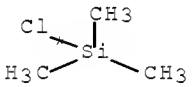
PRO AR 156928-09-5
NTE stereoselective

RX(24) RCT AR 156928-09-5, X 108-24-7
RGT D 121-44-8 Et3N
PRO AT 162119-35-9
CAT 1122-58-3 4-DMAP
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 3 hours, 20 deg C

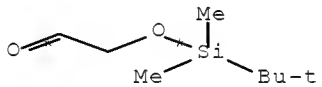
RX(63) OF 80 COMPOSED OF RX(3), RX(23), RX(24)
RX(63) A + J + AI + X ===> AT



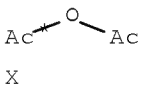
A



J

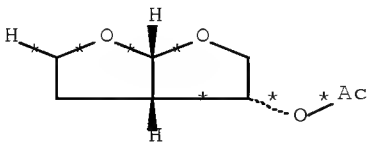


AI



X

3
STEPS



AT
YIELD 72%

RX(3) RCT A 110-63-4, J 75-77-4

STAGE(1)
RGT D 121-44-8 Et3N
CON 2 hours, room temperature

STAGE(2)
RGT G 26412-87-3 Pyridine-SO3 (1:1), D 121-44-8 Et3N
SOL 67-68-5 DMSO
CON SUBSTAGE(1) 0.5 hours, 0 - 5 deg C
SUBSTAGE(2) 4 hours, room temperature

PRO K 72157-18-7

RX(23) RCT K 72157-18-7, AI 102191-92-4

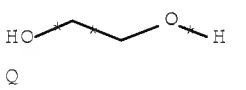
STAGE(1)
CAT 147-85-3 (S)-Proline
SOL 109-99-9 THF
CON 84 hours, 4 deg C

STAGE(2)
RGT AS 7647-01-0 HCl
SOL 7732-18-5 Water
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 18 hours, 4 deg C

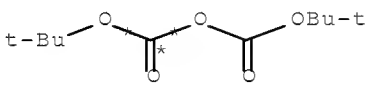
PRO AR 156928-09-5
NTE stereoselective

RX(24) RCT AR 156928-09-5, X 108-24-7
RGT D 121-44-8 Et3N
PRO AT 162119-35-9
CAT 1122-58-3 4-DMAP
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 3 hours, 20 deg C

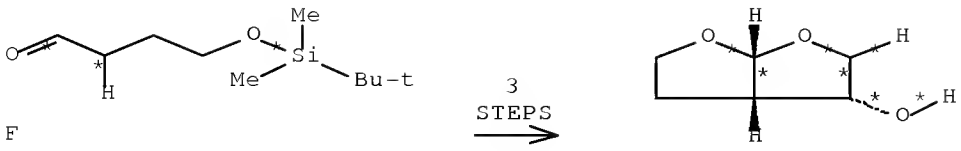
RX(68) OF 80 COMPOSED OF RX(8), RX(9), RX(22)
RX(68) Q + T + F ===> AR



Q



T



F

AR
YIELD 63%

RX(8) RCT Q 107-21-1, T 24424-99-5
RGT V 1122-58-3 4-DMAP
PRO U 305856-92-2
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 0.5 hours, room temperature
SUBSTAGE(2) 24 hours, room temperature

RX(9) RCT U 305856-92-2
RGT G 26412-87-3 Pyridine-SO3 (1:1), D 121-44-8 Et3N
PRO W 1015081-35-2
SOL 75-09-2 CH2Cl2, 67-68-5 DMSO
CON SUBSTAGE(1) 20 minutes, 0 - 10 deg C
SUBSTAGE(2) 1.5 hours, 0 - 10 deg C

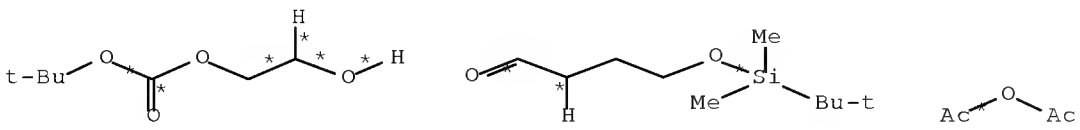
RX(22) RCT F 87184-81-4, W 1015081-35-2

STAGE(1)
CAT 147-85-3 (S)-Proline
SOL 109-99-9 THF
CON 84 hours, 4 deg C

STAGE(2)
RGT AS 7647-01-0 HCl
SOL 7732-18-5 Water
CON 44 hours, 20 deg C

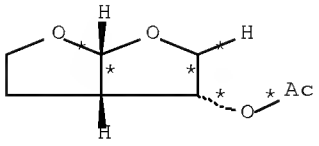
PRO AR 156928-09-5
NTE stereoselective

RX(69) OF 80 COMPOSED OF RX(9), RX(22), RX(24)
RX(69) U + F + X ===> AT



U F X

3
STEPS



AT
YIELD 72%

RX(9) RCT U 305856-92-2
RGT G 26412-87-3 Pyridine-SO3 (1:1), D 121-44-8 Et3N
PRO W 1015081-35-2
SOL 75-09-2 CH2Cl2, 67-68-5 DMSO
CON SUBSTAGE(1) 20 minutes, 0 - 10 deg C
SUBSTAGE(2) 1.5 hours, 0 - 10 deg C

RX(22) RCT F 87184-81-4, W 1015081-35-2

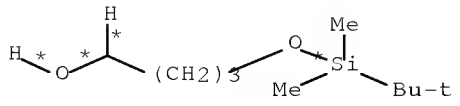
STAGE(1)
CAT 147-85-3 (S)-Proline
SOL 109-99-9 THF
CON 84 hours, 4 deg C

STAGE(2)
RGT AS 7647-01-0 HCl
SOL 7732-18-5 Water
CON 44 hours, 20 deg C

PRO AR 156928-09-5
NTE stereoselective

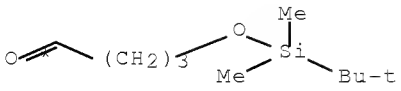
RX(24) RCT AR 156928-09-5, X 108-24-7
RGT D 121-44-8 Et3N
PRO AT 162119-35-9
CAT 1122-58-3 4-DMAP
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 3 hours, 20 deg C

RX(71) OF 80 COMPOSED OF REACTION SEQUENCE RX(2), RX(22)
AND REACTION SEQUENCE RX(8), RX(9), RX(22)
...C ===> F...
...Q + T + F ===> AR



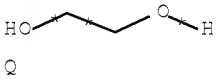
C

3
STEPS

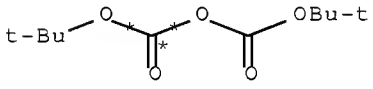


F

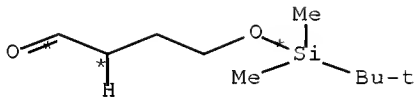
START NEXT REACTION SEQUENCE



Q

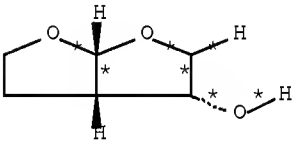


T



F

3 STEPS



AR
YIELD 63%

RX(2) RCT C 87184-99-4
RGT G 26412-87-3 Pyridine-SO3 (1:1), D 121-44-8 Et3N
PRO F 87184-81-4
SOL 108-88-3 PhMe, 67-68-5 DMSO
CON SUBSTAGE(1) 1 hour, 0 - 10 deg C
SUBSTAGE(2) 0.5 hours, 0 - 10 deg C

RX(8) RCT Q 107-21-1, T 24424-99-5
RGT V 1122-58-3 4-DMAP
PRO U 305856-92-2
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 0.5 hours, room temperature
SUBSTAGE(2) 24 hours, room temperature

RX(9) RCT U 305856-92-2
RGT G 26412-87-3 Pyridine-SO3 (1:1), D 121-44-8 Et3N
PRO W 1015081-35-2
SOL 75-09-2 CH2Cl2, 67-68-5 DMSO
CON SUBSTAGE(1) 20 minutes, 0 - 10 deg C
SUBSTAGE(2) 1.5 hours, 0 - 10 deg C

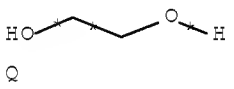
RX(22) RCT F 87184-81-4, W 1015081-35-2

STAGE(1)
CAT 147-85-3 (S)-Proline
SOL 109-99-9 THF
CON 84 hours, 4 deg C

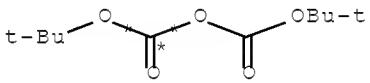
STAGE(2)
RGT AS 7647-01-0 HCl
SOL 7732-18-5 Water
CON 44 hours, 20 deg C

PRO AR 156928-09-5
NTE stereoselective

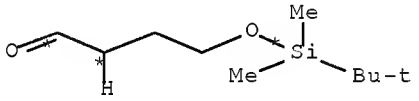
RX(72) OF 80 COMPOSED OF RX(8), RX(9), RX(22), RX(24)
RX(72) Q + T + F + X ===> AT



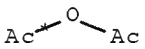
Q



T

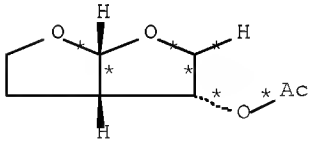


F



X

4
STEPS



AT
YIELD 72%

RX(8) RCT Q 107-21-1, T 24424-99-5
RGT V 1122-58-3 4-DMAP
PRO U 305856-92-2
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 0.5 hours, room temperature
SUBSTAGE(2) 24 hours, room temperature

RX(9) RCT U 305856-92-2
RGT G 26412-87-3 Pyridine-SO3 (1:1), D 121-44-8 Et3N
PRO W 1015081-35-2
SOL 75-09-2 CH2Cl2, 67-68-5 DMSO
CON SUBSTAGE(1) 20 minutes, 0 - 10 deg C
SUBSTAGE(2) 1.5 hours, 0 - 10 deg C

RX(22) RCT F 87184-81-4, W 1015081-35-2

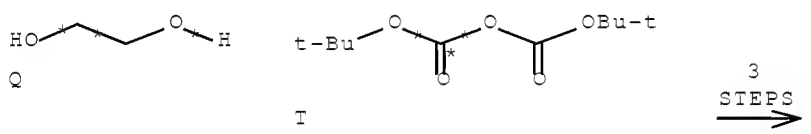
STAGE(1)
CAT 147-85-3 (S)-Proline
SOL 109-99-9 THF
CON 84 hours, 4 deg C

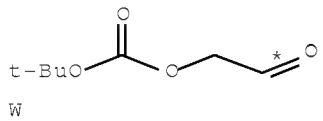
STAGE(2)
RGT AS 7647-01-0 HCl
SOL 7732-18-5 Water
CON 44 hours, 20 deg C

PRO AR 156928-09-5
NTE stereoselective

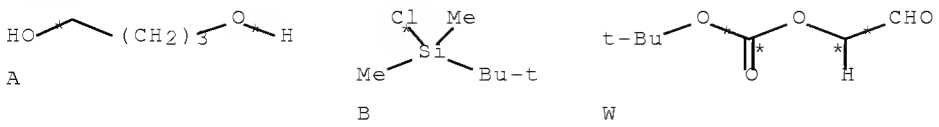
RX(24) RCT AR 156928-09-5, X 108-24-7
RGT D 121-44-8 Et3N
PRO AT 162119-35-9
CAT 1122-58-3 4-DMAP
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 3 hours, 20 deg C

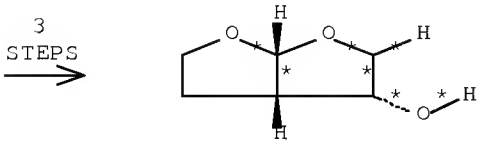
RX(76) OF 80 COMPOSED OF REACTION SEQUENCE RX(8), RX(9), RX(22)
AND REACTION SEQUENCE RX(1), RX(2), RX(22)
...Q + T ===> W...
...A + B + W ===> AR





START NEXT REACTION SEQUENCE





AR
YIELD 63%

RX(8) RCT Q 107-21-1, T 24424-99-5
RGT V 1122-58-3 4-DMAP
PRO U 305856-92-2
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 0.5 hours, room temperature
SUBSTAGE(2) 24 hours, room temperature

RX(9) RCT U 305856-92-2
RGT G 26412-87-3 Pyridine-SO3 (1:1), D 121-44-8 Et3N
PRO W 1015081-35-2
SOL 75-09-2 CH2Cl2, 67-68-5 DMSO
CON SUBSTAGE(1) 20 minutes, 0 - 10 deg C
SUBSTAGE(2) 1.5 hours, 0 - 10 deg C

RX(1) RCT A 110-63-4, B 18162-48-6
RGT D 121-44-8 Et3N
PRO C 87184-99-4
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 45 minutes, room temperature
SUBSTAGE(2) 1 hour, room temperature

RX(2) RCT C 87184-99-4
RGT G 26412-87-3 Pyridine-SO3 (1:1), D 121-44-8 Et3N
PRO F 87184-81-4
SOL 108-88-3 PhMe, 67-68-5 DMSO
CON SUBSTAGE(1) 1 hour, 0 - 10 deg C
SUBSTAGE(2) 0.5 hours, 0 - 10 deg C

RX(22) RCT F 87184-81-4, W 1015081-35-2

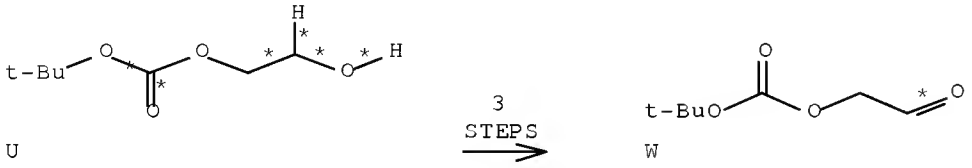
STAGE(1)
CAT 147-85-3 (S)-Proline
SOL 109-99-9 THF
CON 84 hours, 4 deg C

STAGE(2)
RGT AS 7647-01-0 HCl
SOL 7732-18-5 Water

CON 44 hours, 20 deg C

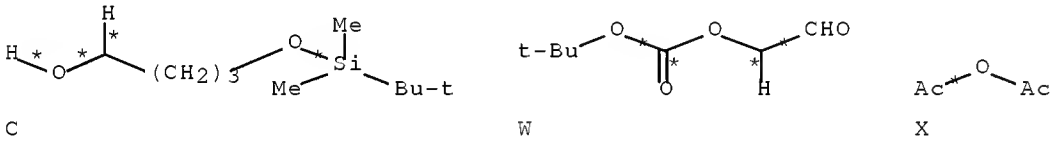
PRO AR 156928-09-5
NTE stereoselective

RX(77) OF 80 COMPOSED OF REACTION SEQUENCE RX(9), RX(22), RX(24)
AND REACTION SEQUENCE RX(2), RX(22), RX(24)
...U ===> W...
...C + W + X ===> AT

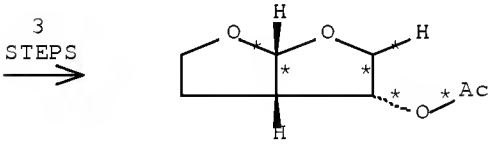


U W

START NEXT REACTION SEQUENCE



C W X



AT
YIELD 72%

RX(9) RCT U 305856-92-2
RGT G 26412-87-3 Pyridine-SO3 (1:1), D 121-44-8 Et3N
PRO W 1015081-35-2
SOL 75-09-2 CH2Cl2, 67-68-5 DMSO
CON SUBSTAGE(1) 20 minutes, 0 - 10 deg C
SUBSTAGE(2) 1.5 hours, 0 - 10 deg C

RX(2) RCT C 87184-99-4
RGT G 26412-87-3 Pyridine-SO3 (1:1), D 121-44-8 Et3N
PRO F 87184-81-4
SOL 108-88-3 PhMe, 67-68-5 DMSO
CON SUBSTAGE(1) 1 hour, 0 - 10 deg C
SUBSTAGE(2) 0.5 hours, 0 - 10 deg C

RX(22) RCT F 87184-81-4, W 1015081-35-2

STAGE(1)
CAT 147-85-3 (S)-Proline
SOL 109-99-9 THF
CON 84 hours, 4 deg C

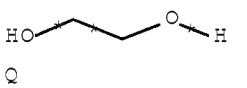
STAGE(2)
RGT AS 7647-01-0 HCl
SOL 7732-18-5 Water
CON 44 hours, 20 deg C

PRO AR 156928-09-5
NTE stereoselective

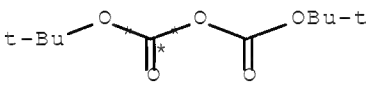
RX(24) RCT AR 156928-09-5, X 108-24-7
RGT D 121-44-8 Et3N
PRO AT 162119-35-9
CAT 1122-58-3 4-DMAP
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 3 hours, 20 deg C

RX(78) OF 80 COMPOSED OF REACTION SEQUENCE RX(8), RX(9), RX(22), RX(24)
AND REACTION SEQUENCE RX(2), RX(22), RX(24)

...Q + T ===> W...
...C + W + X ===> AT

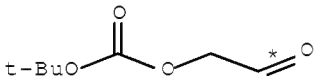


Q



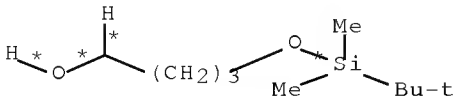
T

3
STEPS

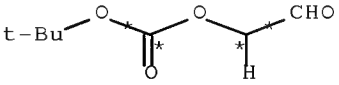


W

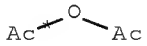
START NEXT REACTION SEQUENCE



C

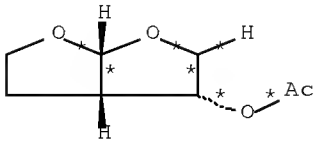


W



X

3
STEPS



AT
YIELD 72%

RX(8) RCT Q 107-21-1, T 24424-99-5
RGT V 1122-58-3 4-DMAP
PRO U 305856-92-2
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 0.5 hours, room temperature
SUBSTAGE(2) 24 hours, room temperature

RX(9) RCT U 305856-92-2
RGT G 26412-87-3 Pyridine-SO3 (1:1), D 121-44-8 Et3N
PRO W 1015081-35-2
SOL 75-09-2 CH2Cl2, 67-68-5 DMSO
CON SUBSTAGE(1) 20 minutes, 0 - 10 deg C
SUBSTAGE(2) 1.5 hours, 0 - 10 deg C

RX(2) RCT C 87184-99-4
RGT G 26412-87-3 Pyridine-SO3 (1:1), D 121-44-8 Et3N
PRO F 87184-81-4
SOL 108-88-3 PhMe, 67-68-5 DMSO
CON SUBSTAGE(1) 1 hour, 0 - 10 deg C
SUBSTAGE(2) 0.5 hours, 0 - 10 deg C

RX(22) RCT F 87184-81-4, W 1015081-35-2

STAGE(1)
CAT 147-85-3 (S)-Proline
SOL 109-99-9 THF
CON 84 hours, 4 deg C

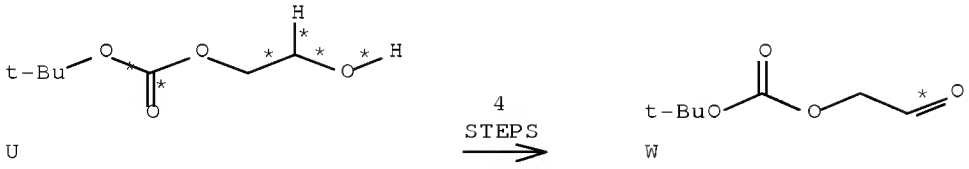
STAGE(2)
RGT AS 7647-01-0 HCl
SOL 7732-18-5 Water
CON 44 hours, 20 deg C

PRO AR 156928-09-5
NTE stereoselective

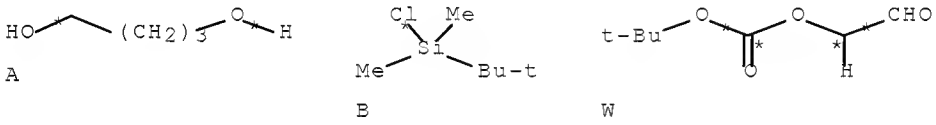
RX(24) RCT AR 156928-09-5, X 108-24-7
RGT D 121-44-8 Et3N
PRO AT 162119-35-9
CAT 1122-58-3 4-DMAP
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 3 hours, 20 deg C

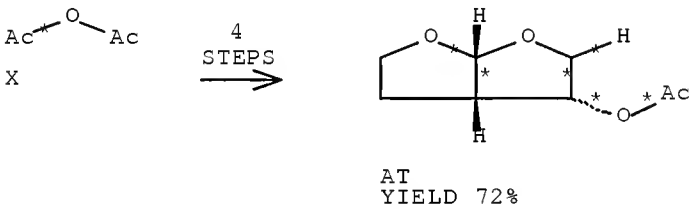
RX(79) OF 80 COMPOSED OF REACTION SEQUENCE RX(9), RX(22), RX(24)
AND REACTION SEQUENCE RX(1), RX(2), RX(22), RX(24)

...U ===> W...
...A + B + W + X ===> AT



START NEXT REACTION SEQUENCE





AT
YIELD 72%

RX(9) RCT U 305856-92-2
RGT G 26412-87-3 Pyridine-SO3 (1:1), D 121-44-8 Et3N
PRO W 1015081-35-2
SOL 75-09-2 CH2Cl2, 67-68-5 DMSO
CON SUBSTAGE(1) 20 minutes, 0 - 10 deg C
SUBSTAGE(2) 1.5 hours, 0 - 10 deg C

RX(1) RCT A 110-63-4, B 18162-48-6
RGT D 121-44-8 Et3N
PRO C 87184-99-4
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 45 minutes, room temperature
SUBSTAGE(2) 1 hour, room temperature

RX(2) RCT C 87184-99-4
RGT G 26412-87-3 Pyridine-SO3 (1:1), D 121-44-8 Et3N
PRO F 87184-81-4
SOL 108-88-3 PhMe, 67-68-5 DMSO
CON SUBSTAGE(1) 1 hour, 0 - 10 deg C
SUBSTAGE(2) 0.5 hours, 0 - 10 deg C

RX(22) RCT F 87184-81-4, W 1015081-35-2

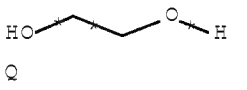
STAGE(1)
CAT 147-85-3 (S)-Proline
SOL 109-99-9 THF
CON 84 hours, 4 deg C

STAGE(2)
RGT AS 7647-01-0 HCl
SOL 7732-18-5 Water
CON 44 hours, 20 deg C

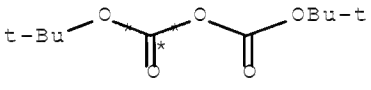
PRO AR 156928-09-5
NTE stereoselective

RX(24) RCT AR 156928-09-5, X 108-24-7
RGT D 121-44-8 Et3N
PRO AT 162119-35-9
CAT 1122-58-3 4-DMAP
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 3 hours, 20 deg C

RX(80) OF 80 COMPOSED OF REACTION SEQUENCE RX(8), RX(9), RX(22), RX(24)
AND REACTION SEQUENCE RX(1), RX(2), RX(22), RX(24)
...Q + T ===> W...
...A + B + W + X ===> AT

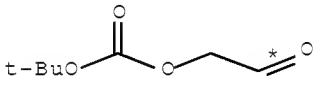


Q



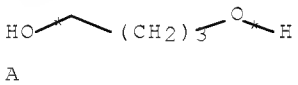
T

4
STEPS



W

START NEXT REACTION SEQUENCE



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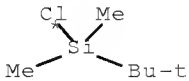

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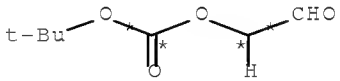
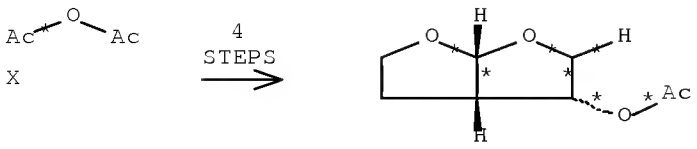


W



AT
YIELD 72%

RX(8) RCT Q 107-21-1, T 24424-99-5
RGT V 1122-58-3 4-DMAP
PRO U 305856-92-2
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 0.5 hours, room temperature
SUBSTAGE(2) 24 hours, room temperature

RX(9) RCT U 305856-92-2
RGT G 26412-87-3 Pyridine-SO3 (1:1), D 121-44-8 Et3N
PRO W 1015081-35-2
SOL 75-09-2 CH2Cl2, 67-68-5 DMSO
CON SUBSTAGE(1) 20 minutes, 0 - 10 deg C
SUBSTAGE(2) 1.5 hours, 0 - 10 deg C

RX(1) RCT A 110-63-4, B 18162-48-6
RGT D 121-44-8 Et3N
PRO C 87184-99-4
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 45 minutes, room temperature
SUBSTAGE(2) 1 hour, room temperature

RX(2) RCT C 87184-99-4
RGT G 26412-87-3 Pyridine-SO3 (1:1), D 121-44-8 Et3N
PRO F 87184-81-4
SOL 108-88-3 PhMe, 67-68-5 DMSO
CON SUBSTAGE(1) 1 hour, 0 - 10 deg C
SUBSTAGE(2) 0.5 hours, 0 - 10 deg C

RX(22) RCT F 87184-81-4, W 1015081-35-2

STAGE(1)
CAT 147-85-3 (S)-Proline
SOL 109-99-9 THF
CON 84 hours, 4 deg C

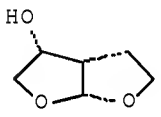
STAGE(2)
RGT AS 7647-01-0 HCl
SOL 7732-18-5 Water
CON 44 hours, 20 deg C

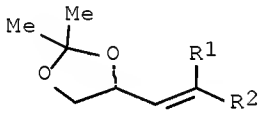
PRO AR 156928-09-5
NTE stereoselective

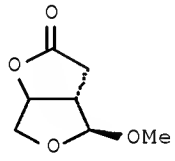
RX(24) RCT AR 156928-09-5, X 108-24-7
RGT D 121-44-8 Et3N
PRO AT 162119-35-9
CAT 1122-58-3 4-DMAP

SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 3 hours, 20 deg C
AN 148:379603 CASREACT Full-text

L71 ANSWER 2 OF 3 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 144:170908 CASREACT Full-text
TITLE: Stereoselective and Efficient Synthesis of (3R,3aS,6aR)-Hexahydrofuro[2,3-b]furan-3-ol
AUTHOR(S): Quaedflieg, Peter J. L. M.; Kesteleyn, Bart R. R.; Wigerinck, Piet B. T. P.; Goyvaerts, Nicolaas M. F.; Vijn, Robert Jan; Liebregts, Constantinus S. M.; Kooistra, Jaap H. M. H.; Cusan, Claudia
CORPORATE SOURCE: LS-ASCD, DSM Pharma Chemicals, Geleen, 6160 MD, Neth.
SOURCE: Organic Letters (2005), 7(26), 5917-5920
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

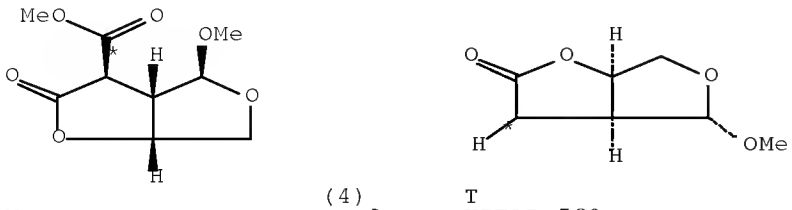

I


II


III

AB Two short and efficient synthesis routes have been developed for (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-ol I, a key building block of the investigational HIV protease inhibitor TMC114, using (S)-2,3-O- isopropylideneglyceraldehyde as the source of chirality. Both routes are based on a diastereoselective Michael addition of nitromethane to α,β-unsatd. esters II (R1 = R2 = MeO2C; R1 = H, R2 = EtO2C), which gave predominantly the syn congeners, followed by a Nef oxidation and cyclization to afford lactone acetal III, which was reduced and cyclized to give I.
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(4) OF 23 ...M ===> T...


M (4) T
YIELD 52%

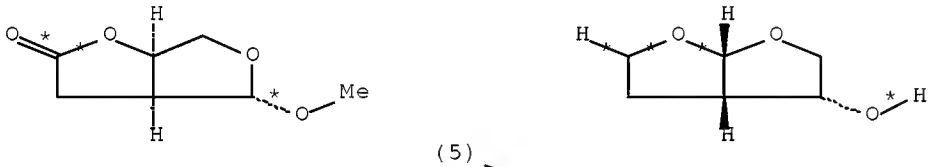
RX(4) RCT M 874290-09-2

STAGE(1)
RGT U 1310-58-3 KOH
SOL 7732-18-5 Water, 67-56-1 MeOH
CON 2 hours, reflux

STAGE(2)
RGT V 64-19-7 AcOH
CON 35 deg C

PRO T 866594-60-7
NTE stereoselective, alternative prepn. gave lower stereoselectivity

RX(5) OF 23 ...T ===> W



T

W
YIELD 76%

RX(5) RCT T 866594-60-7

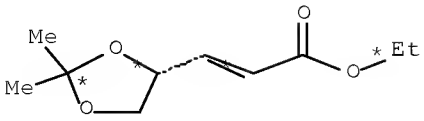
STAGE(1)
RGT X 16949-15-8 LiBH4
SOL 109-99-9 THF
CON SUBSTAGE(1) 0.5 hours, room temperature
SUBSTAGE(2) 2.5 hours, 50 deg C

STAGE(2)
RGT Y 7647-01-0 HCl
SOL 7732-18-5 Water
CON SUBSTAGE(1) 4 hours, -10 - -5 deg C
SUBSTAGE(2) 2 hours, -10 deg C

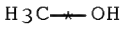
STAGE(3)
RGT Z 121-44-8 Et3N
CON 1 hour, <0 deg C

PRO W 156928-09-5
NTE stereoselective

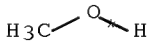
RX(6) OF 23 ...C + 2 R ===> T...



C

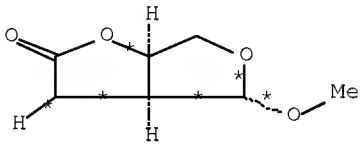


R



R

(6) →



T
YIELD 50%

RX(6) RCT C 104321-62-2, R 67-56-1

STAGE(1)
RGT K 75-52-5 MeNO2, O 6674-22-2 DBU
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 0.6 hours, 10 - 21 deg C
SUBSTAGE(2) 18 hours, 20 deg C

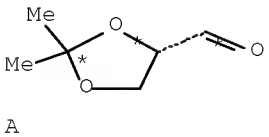
STAGE(2)
RGT L 124-41-4 NaOMe
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 35 minutes, 0 deg C
SUBSTAGE(2) 30 minutes, 0 deg C

STAGE(3)
RGT P 7664-93-9 H2SO4
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 3 hours, 0 - 5 deg C
SUBSTAGE(2) 2 hours, 0 - 2 deg C

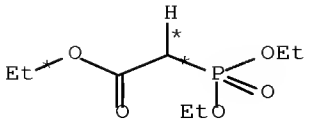
STAGE(4)
RGT AA 298-14-6 KHCO3
SOL 7732-18-5 Water
CON 1 hour, 0 - 6 deg C, pH 7

PRO T 866594-60-7
NTE stereoselective, other diastereomer also detected, 3.75:1 diastereomeric ratio, safety, alternative prepn. also described

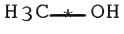
RX(8) OF 23 COMPOSED OF RX(1), RX(6)
RX(8) A + B + 2 R ===> T



A



B



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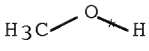
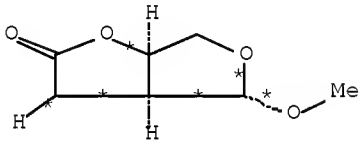


R

2
STEPS



T
YIELD 50%

RX(1) RCT A 22323-80-4, B 867-13-0

STAGE(1)
SOL 7732-18-5 Water, 109-99-9 THF
CON 25 minutes, 13 - 17 deg C

STAGE(2)
RGT D 584-08-7 K2CO3
CON SUBSTAGE(1) 0.5 hours, 17 - 25 deg C
SUBSTAGE(2) 17 hours, 20 deg C, pH 11.6

PRO C 104321-62-2
NTE stereoselective

RX(6) RCT C 104321-62-2, R 67-56-1

STAGE(1)
RGT K 75-52-5 MeNO2, O 6674-22-2 DBU
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 0.6 hours, 10 - 21 deg C
SUBSTAGE(2) 18 hours, 20 deg C

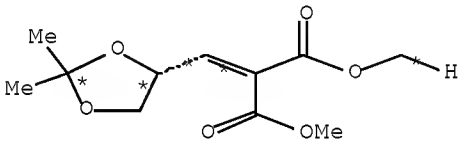
STAGE(2)
RGT L 124-41-4 NaOMe
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 35 minutes, 0 deg C
SUBSTAGE(2) 30 minutes, 0 deg C

STAGE(3)
RGT P 7664-93-9 H2SO4
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 3 hours, 0 - 5 deg C
SUBSTAGE(2) 2 hours, 0 - 2 deg C

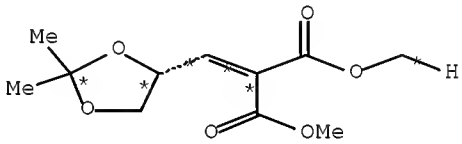
STAGE(4)
RGT AA 298-14-6 KHCO3
SOL 7732-18-5 Water
CON 1 hour, 0 - 6 deg C, pH 7

PRO T 866594-60-7
NTE stereoselective, other diastereomer also detected, 3.75:1 diastereomeric ratio, safety, alternative prepn. also described

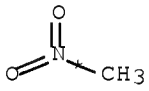
RX(10) OF 23 COMPOSED OF RX(3), RX(4)
RX(10) 2 H + 2 K + 2 L ===> T



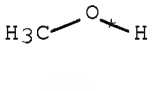
H



H



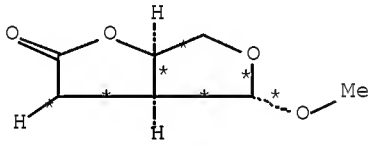
2 K



Na

2 L

2
STEPS



T
YIELD 52%

RX(3) RCT H 204390-79-4, K 75-52-5

STAGE(1)
RGT O 6674-22-2 DBU
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 0.5 hours, 0 - 25 deg C
SUBSTAGE(2) 3 hours, 20 deg C

STAGE(2)
RCT L 124-41-4
SOL 67-56-1 MeOH
CON 30 minutes, 0 - 3 deg C

STAGE(3)
RGT P 7664-93-9 H2SO4
SOL 67-56-1 MeOH

CON 5 hours, 0 - 3 deg C

STAGE(4)
RGT Q 144-55-8 NaHCO3
SOL 7732-18-5 Water, 141-78-6 AcOEt
CON 0 - 15 deg C, pH 6.5 - 7

PRO M 874290-09-2, N 874290-10-5
NTE stereoselective, traces of other diastereomers also detected

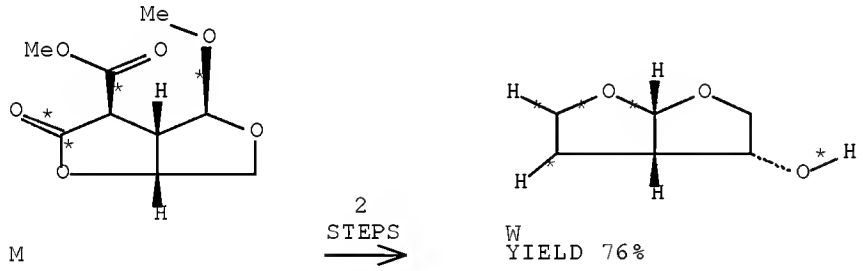
RX(4) RCT M 874290-09-2

STAGE(1)
RGT U 1310-58-3 KOH
SOL 7732-18-5 Water, 67-56-1 MeOH
CON 2 hours, reflux

STAGE(2)
RGT V 64-19-7 AcOH
CON 35 deg C

PRO T 866594-60-7
NTE stereoselective, alternative prepn. gave lower stereoselectivity

RX(11) OF 23 COMPOSED OF RX(4), RX(5)
RX(11) M ===> W



M

W
YIELD 76%

RX(4) RCT M 874290-09-2

STAGE(1)
RGT U 1310-58-3 KOH
SOL 7732-18-5 Water, 67-56-1 MeOH
CON 2 hours, reflux

STAGE(2)
RGT V 64-19-7 AcOH
CON 35 deg C

PRO T 866594-60-7
NTE stereoselective, alternative prepn. gave lower stereoselectivity

RX(5) RCT T 866594-60-7

STAGE(1)

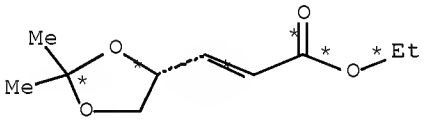
RGT X 16949-15-8 LiBH4
SOL 109-99-9 THF
CON SUBSTAGE(1) 0.5 hours, room temperature
SUBSTAGE(2) 2.5 hours, 50 deg C

STAGE(2)
RGT Y 7647-01-0 HCl
SOL 7732-18-5 Water
CON SUBSTAGE(1) 4 hours, -10 - -5 deg C
SUBSTAGE(2) 2 hours, -10 deg C

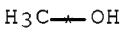
STAGE(3)
RGT Z 121-44-8 Et3N
CON 1 hour, <0 deg C

PRO W 156928-09-5
NTE stereoselective

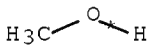
RX(12) OF 23 COMPOSED OF RX(6), RX(5)
RX(12) C + 2 R ===> W



C

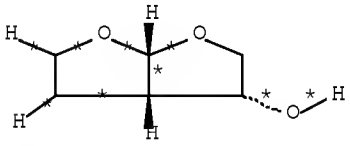


R



R

2 STEPS



W
YIELD 76%

RX(6) RCT C 104321-62-2, R 67-56-1

STAGE(1)
RGT K 75-52-5 MeNO2, O 6674-22-2 DBU
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 0.6 hours, 10 - 21 deg C
SUBSTAGE(2) 18 hours, 20 deg C

STAGE(2)
RGT L 124-41-4 NaOMe
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 35 minutes, 0 deg C
SUBSTAGE(2) 30 minutes, 0 deg C

STAGE(3)
RGT P 7664-93-9 H2SO4
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 3 hours, 0 - 5 deg C
SUBSTAGE(2) 2 hours, 0 - 2 deg C

STAGE(4)
RGT AA 298-14-6 KHCO3
SOL 7732-18-5 Water
CON 1 hour, 0 - 6 deg C, pH 7

PRO T 866594-60-7
NTE stereoselective, other diastereomer also detected, 3.75:1 diastereomeric ratio, safety, alternative prepn. also described

RX(5) RCT T 866594-60-7

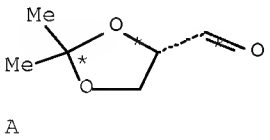
STAGE(1)
RGT X 16949-15-8 LiBH4
SOL 109-99-9 THF
CON SUBSTAGE(1) 0.5 hours, room temperature
SUBSTAGE(2) 2.5 hours, 50 deg C

STAGE(2)
RGT Y 7647-01-0 HCl
SOL 7732-18-5 Water
CON SUBSTAGE(1) 4 hours, -10 - -5 deg C
SUBSTAGE(2) 2 hours, -10 deg C

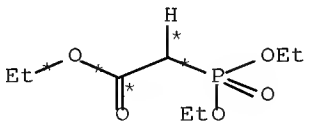
STAGE(3)
RGT Z 121-44-8 Et3N
CON 1 hour, <0 deg C

PRO W 156928-09-5
NTE stereoselective

RX(15) OF 23 COMPOSED OF RX(1), RX(6), RX(5)
RX(15) A + B + 2 R ===> W



A



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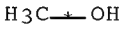

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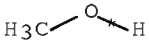
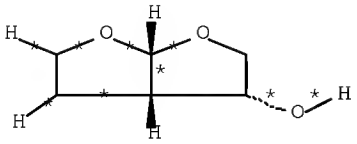


R

3 STEPS →



W
YIELD 76%

RX(1) RCT A 22323-80-4, B 867-13-0

STAGE(1)
SOL 7732-18-5 Water, 109-99-9 THF
CON 25 minutes, 13 - 17 deg C

STAGE(2)
RGT D 584-08-7 K2CO3
CON SUBSTAGE(1) 0.5 hours, 17 - 25 deg C
SUBSTAGE(2) 17 hours, 20 deg C, pH 11.6

PRO C 104321-62-2
NTE stereoselective

RX(6) RCT C 104321-62-2, R 67-56-1

STAGE(1)
RGT K 75-52-5 MeNO2, O 6674-22-2 DBU
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 0.6 hours, 10 - 21 deg C
SUBSTAGE(2) 18 hours, 20 deg C

STAGE(2)
RGT L 124-41-4 NaOMe
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 35 minutes, 0 deg C
SUBSTAGE(2) 30 minutes, 0 deg C

STAGE(3)
RGT P 7664-93-9 H2SO4
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 3 hours, 0 - 5 deg C
SUBSTAGE(2) 2 hours, 0 - 2 deg C

STAGE(4)
RGT AA 298-14-6 KHCO3
SOL 7732-18-5 Water
CON 1 hour, 0 - 6 deg C, pH 7

PRO T 866594-60-7
NTE stereoselective, other diastereomer also detected, 3.75:1 diastereomeric ratio, safety, alternative prepn. also described

RX(5) RCT T 866594-60-7

STAGE(1)
RGT X 16949-15-8 LiBH4

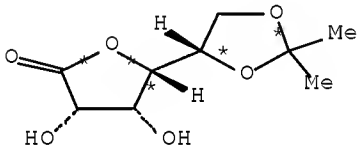
SOL 109-99-9 THF
CON SUBSTAGE(1) 0.5 hours, room temperature
SUBSTAGE(2) 2.5 hours, 50 deg C

STAGE(2)
RGT Y 7647-01-0 HCl
SOL 7732-18-5 Water
CON SUBSTAGE(1) 4 hours, -10 - -5 deg C
SUBSTAGE(2) 2 hours, -10 deg C

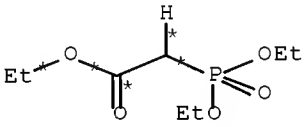
STAGE(3)
RGT Z 121-44-8 Et3N
CON 1 hour, <0 deg C

PRO W 156928-09-5
NTE stereoselective

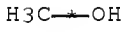
RX(16) OF 23 COMPOSED OF RX(7), RX(1), RX(6), RX(5)
RX(16) AB + B + 2 R ===> W



AB



B



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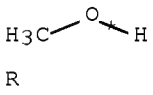
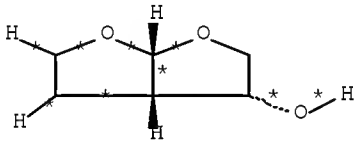


R

4
STEPS



W
YIELD 76%

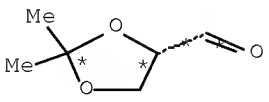
RX(7) RCT AB 94697-68-4
RGT AC 7790-21-8 KIO4, AA 298-14-6 KHCO3
PRO A 22323-80-4
SOL 7732-18-5 Water, 109-99-9 THF
CON SUBSTAGE(1) 3 hours, 32 - 34 deg C
SUBSTAGE(2) 4.5 hours, 32 deg C

RX(1) RCT A 22323-80-4, B 867-13-0

STAGE(1)
SOL 7732-18-5 Water, 109-99-9 THF
CON 25 minutes, 13 - 17 deg C

```
            STAGE(2)
               RGT  D 584-08-7 K2CO3
               CON  SUBSTAGE(1) 0.5 hours, 17 - 25 deg C
                    SUBSTAGE(2) 17 hours, 20 deg C, pH 11.6

            PRO  C 104321-62-2
            NTE  stereoselective

RX(6)       RCT  C 104321-62-2, R 67-56-1

            STAGE(1)
               RGT  K 75-52-5 MeNO2, O 6674-22-2 DBU
               SOL  67-56-1 MeOH
               CON  SUBSTAGE(1) 0.6 hours, 10 - 21 deg C
                    SUBSTAGE(2) 18 hours, 20 deg C

            STAGE(2)
               RGT  L 124-41-4 NaOMe
               SOL  67-56-1 MeOH
               CON  SUBSTAGE(1) 35 minutes, 0 deg C
                    SUBSTAGE(2) 30 minutes, 0 deg C

            STAGE(3)
               RGT  P 7664-93-9 H2SO4
               SOL  67-56-1 MeOH
               CON  SUBSTAGE(1) 3 hours, 0 - 5 deg C
                    SUBSTAGE(2) 2 hours, 0 - 2 deg C

            STAGE(4)
               RGT  AA 298-14-6 KHCO3
               SOL  7732-18-5 Water
               CON  1 hour, 0 - 6 deg C, pH 7

            PRO  T 866594-60-7
            NTE  stereoselective, other diastereomer also detected, 3.75:1
                 diastereomeric ratio, safety, alternative prepn. also described

RX(5)       RCT  T 866594-60-7

            STAGE(1)
               RGT  X 16949-15-8 LiBH4
               SOL  109-99-9 THF
               CON  SUBSTAGE(1) 0.5 hours, room temperature
                    SUBSTAGE(2) 2.5 hours, 50 deg C

            STAGE(2)
               RGT  Y 7647-01-0 HCl
               SOL  7732-18-5 Water
               CON  SUBSTAGE(1) 4 hours, -10 - -5 deg C
                    SUBSTAGE(2) 2 hours, -10 deg C

            STAGE(3)
               RGT  Z 121-44-8 Et3N
               CON  1 hour, <0 deg C

            PRO  W 156928-09-5
            NTE  stereoselective


RX(17) OF 23 COMPOSED OF RX(2), RX(3), RX(4)
```

RX(17) 2 A + 2 G + 2 K + 2 L ===> T



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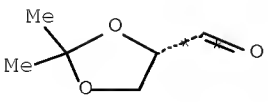
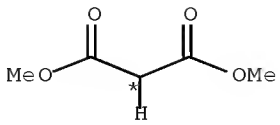


A



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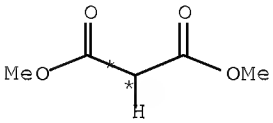

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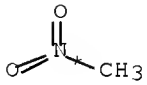
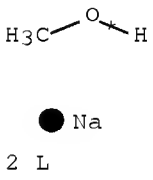
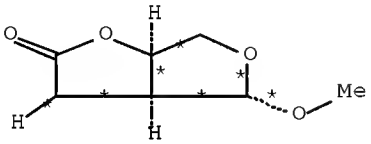


2 K



2 L

3 STEPS



T
YIELD 52%

RX(2) RCT A 22323-80-4, G 108-59-8

STAGE(1)
SOL 109-99-9 THF
CON 3 hours, 20 deg C

STAGE(2)
RGT I 110-86-1 Pyridine
CON 20 hours

STAGE(3)
RGT J 108-24-7 Ac2O
SOL 109-99-9 THF
CON SUBSTAGE(1) 4 hours, 45 deg C
SUBSTAGE(2) 12 hours, 45 deg C

PRO H 204390-79-4

RX(3) RCT H 204390-79-4, K 75-52-5

STAGE(1)
RGT O 6674-22-2 DBU
SOL 67-56-1 MeOH

CON SUBSTAGE(1) 0.5 hours, 0 - 25 deg C
SUBSTAGE(2) 3 hours, 20 deg C

STAGE(2)
RCT L 124-41-4
SOL 67-56-1 MeOH
CON 30 minutes, 0 - 3 deg C

STAGE(3)
RGT P 7664-93-9 H2SO4
SOL 67-56-1 MeOH
CON 5 hours, 0 - 3 deg C

STAGE(4)
RGT Q 144-55-8 NaHCO3
SOL 7732-18-5 Water, 141-78-6 AcOEt
CON 0 - 15 deg C, pH 6.5 - 7

PRO M 874290-09-2, N 874290-10-5
NTE stereoselective, traces of other diastereomers also detected

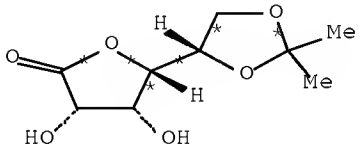
RX(4) RCT M 874290-09-2

STAGE(1)
RGT U 1310-58-3 KOH
SOL 7732-18-5 Water, 67-56-1 MeOH
CON 2 hours, reflux

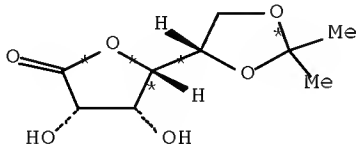
STAGE(2)
RGT V 64-19-7 AcOH
CON 35 deg C

PRO T 866594-60-7
NTE stereoselective, alternative prepn. gave lower stereoselectivity

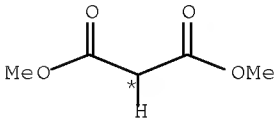
RX(18) OF 23 COMPOSED OF RX(7), RX(2), RX(3), RX(4)
RX(18) 2 AB + 2 G + 2 K + 2 L ===> T



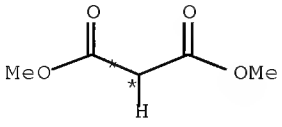
AB



AB



G



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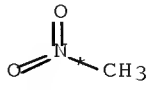
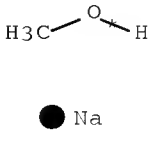
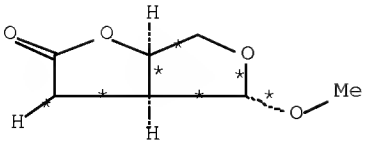


2 K



2 L

4
STEPS



T
YIELD 52%

RX(7) RCT AB 94697-68-4
RGT AC 7790-21-8 KIO4, AA 298-14-6 KHCO3
PRO A 22323-80-4
SOL 7732-18-5 Water, 109-99-9 THF
CON SUBSTAGE(1) 3 hours, 32 - 34 deg C
SUBSTAGE(2) 4.5 hours, 32 deg C

RX(2) RCT A 22323-80-4, G 108-59-8

STAGE(1)
SOL 109-99-9 THF
CON 3 hours, 20 deg C

STAGE(2)
RGT I 110-86-1 Pyridine
CON 20 hours

STAGE(3)
RGT J 108-24-7 Ac2O
SOL 109-99-9 THF
CON SUBSTAGE(1) 4 hours, 45 deg C
SUBSTAGE(2) 12 hours, 45 deg C

PRO H 204390-79-4

RX(3) RCT H 204390-79-4, K 75-52-5

STAGE(1)
RGT O 6674-22-2 DBU
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 0.5 hours, 0 - 25 deg C
SUBSTAGE(2) 3 hours, 20 deg C

STAGE(2)
RCT L 124-41-4
SOL 67-56-1 MeOH
CON 30 minutes, 0 - 3 deg C

STAGE(3)
RGT P 7664-93-9 H2SO4
SOL 67-56-1 MeOH
CON 5 hours, 0 - 3 deg C

STAGE(4)
RGT Q 144-55-8 NaHCO3
SOL 7732-18-5 Water, 141-78-6 AcOEt
CON 0 - 15 deg C, pH 6.5 - 7

PRO M 874290-09-2, N 874290-10-5
NTE stereoselective, traces of other diastereomers also detected

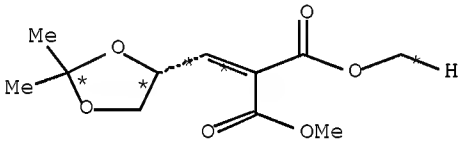
RX(4) RCT M 874290-09-2

STAGE(1)
RGT U 1310-58-3 KOH
SOL 7732-18-5 Water, 67-56-1 MeOH
CON 2 hours, reflux

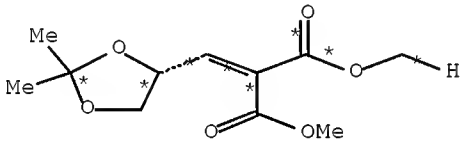
STAGE(2)
RGT V 64-19-7 AcOH
CON 35 deg C

PRO T 866594-60-7
NTE stereoselective, alternative prepn. gave lower stereoselectivity

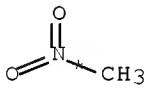
RX(19) OF 23 COMPOSED OF RX(3), RX(4), RX(5)
RX(19) 2 H + 2 K + 2 L ===> W



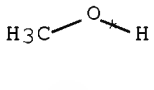
H



H



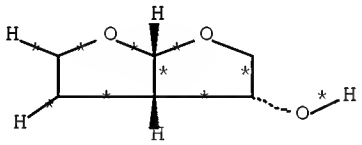
2 K



Na

2 L

3
STEPS



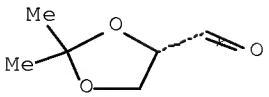
W
YIELD 76%

RX(3) RCT H 204390-79-4, K 75-52-5

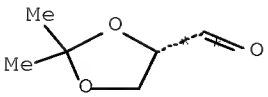
STAGE(1)
RGT O 6674-22-2 DBU
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 0.5 hours, 0 - 25 deg C
SUBSTAGE(2) 3 hours, 20 deg C

STAGE(2)
RCT L 124-41-4

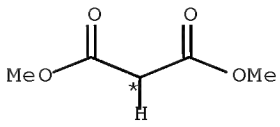
```
                SOL  67-56-1 MeOH
                CON  30 minutes, 0 - 3 deg C

              STAGE(3)
                RGT  P 7664-93-9 H2SO4
                SOL  67-56-1 MeOH
                CON  5 hours, 0 - 3 deg C

              STAGE(4)
                RGT  Q 144-55-8 NaHCO3
                SOL  7732-18-5 Water, 141-78-6 AcOEt
                CON  0 - 15 deg C, pH 6.5 - 7

            PRO  M 874290-09-2, N 874290-10-5
            NTE  stereoselective, traces of other diastereomers also detected

RX(4)       RCT  M 874290-09-2

              STAGE(1)
                RGT  U 1310-58-3 KOH
                SOL  7732-18-5 Water, 67-56-1 MeOH
                CON  2 hours, reflux

              STAGE(2)
                RGT  V 64-19-7 AcOH
                CON  35 deg C

            PRO  T 866594-60-7
            NTE  stereoselective, alternative prepn. gave lower stereoselectivity

RX(5)       RCT  T 866594-60-7

              STAGE(1)
                RGT  X 16949-15-8 LiBH4
                SOL  109-99-9 THF
                CON  SUBSTAGE(1) 0.5 hours, room temperature
                     SUBSTAGE(2) 2.5 hours, 50 deg C

              STAGE(2)
                RGT  Y 7647-01-0 HCl
                SOL  7732-18-5 Water
                CON  SUBSTAGE(1) 4 hours, -10 - -5 deg C
                     SUBSTAGE(2) 2 hours, -10 deg C

              STAGE(3)
                RGT  Z 121-44-8 Et3N
                CON  1 hour, <0 deg C

            PRO  W 156928-09-5
            NTE  stereoselective


RX(20) OF 23 COMPOSED OF RX(2), RX(3), RX(4), RX(5)
RX(20)    2 A  +  2 G  +  2 K  +  2 L  ===>  W
```



A



A



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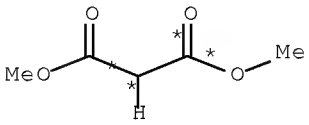

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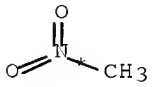

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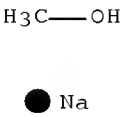

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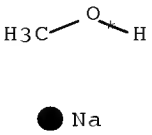

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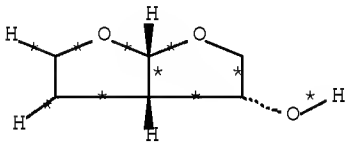
4 STEPS



W
YIELD 76%

RX(2) RCT A 22323-80-4, G 108-59-8

STAGE(1)
SOL 109-99-9 THF
CON 3 hours, 20 deg C

STAGE(2)
RGT I 110-86-1 Pyridine
CON 20 hours

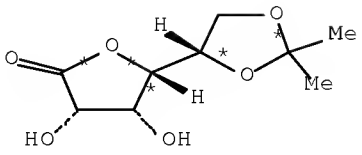
STAGE(3)
RGT J 108-24-7 Ac2O
SOL 109-99-9 THF
CON SUBSTAGE(1) 4 hours, 45 deg C
SUBSTAGE(2) 12 hours, 45 deg C

PRO H 204390-79-4

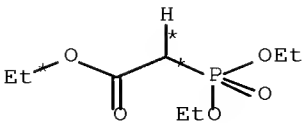
RX(3) RCT H 204390-79-4, K 75-52-5

STAGE(1)
RGT O 6674-22-2 DBU
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 0.5 hours, 0 - 25 deg C

```
                    SUBSTAGE(2) 3 hours, 20 deg C

            STAGE(2)
               RCT  L 124-41-4
               SOL  67-56-1 MeOH
               CON  30 minutes, 0 - 3 deg C

            STAGE(3)
               RGT  P 7664-93-9 H2SO4
               SOL  67-56-1 MeOH
               CON  5 hours, 0 - 3 deg C

            STAGE(4)
               RGT  Q 144-55-8 NaHCO3
               SOL  7732-18-5 Water, 141-78-6 AcOEt
               CON  0 - 15 deg C, pH 6.5 - 7

          PRO  M 874290-09-2, N 874290-10-5
          NTE  stereoselective, traces of other diastereomers also detected

RX(4)     RCT  M 874290-09-2

            STAGE(1)
               RGT  U 1310-58-3 KOH
               SOL  7732-18-5 Water, 67-56-1 MeOH
               CON  2 hours, reflux

            STAGE(2)
               RGT  V 64-19-7 AcOH
               CON  35 deg C

          PRO  T 866594-60-7
          NTE  stereoselective, alternative prepn. gave lower stereoselectivity

RX(5)     RCT  T 866594-60-7

            STAGE(1)
               RGT  X 16949-15-8 LiBH4
               SOL  109-99-9 THF
               CON  SUBSTAGE(1) 0.5 hours, room temperature
                    SUBSTAGE(2) 2.5 hours, 50 deg C

            STAGE(2)
               RGT  Y 7647-01-0 HCl
               SOL  7732-18-5 Water
               CON  SUBSTAGE(1) 4 hours, -10 - -5 deg C
                    SUBSTAGE(2) 2 hours, -10 deg C

            STAGE(3)
               RGT  Z 121-44-8 Et3N
               CON  1 hour, <0 deg C

          PRO  W 156928-09-5
          NTE  stereoselective


RX(21) OF 23 COMPOSED OF RX(7), RX(1), RX(6)
RX(21)    AB  +  B  +  2 R  ===>  T
```



AB



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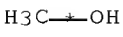

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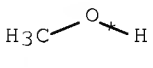
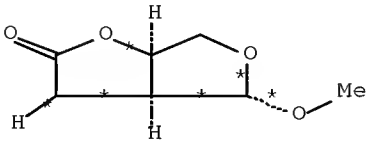


R

3 STEPS



T
YIELD 50%

RX(7) RCT AB 94697-68-4
RGT AC 7790-21-8 KIO4, AA 298-14-6 KHCO3
PRO A 22323-80-4
SOL 7732-18-5 Water, 109-99-9 THF
CON SUBSTAGE(1) 3 hours, 32 - 34 deg C
SUBSTAGE(2) 4.5 hours, 32 deg C

RX(1) RCT A 22323-80-4, B 867-13-0

STAGE(1)
SOL 7732-18-5 Water, 109-99-9 THF
CON 25 minutes, 13 - 17 deg C

STAGE(2)
RGT D 584-08-7 K2CO3
CON SUBSTAGE(1) 0.5 hours, 17 - 25 deg C
SUBSTAGE(2) 17 hours, 20 deg C, pH 11.6

PRO C 104321-62-2
NTE stereoselective

RX(6) RCT C 104321-62-2, R 67-56-1

STAGE(1)
RGT K 75-52-5 MeNO2, O 6674-22-2 DBU
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 0.6 hours, 10 - 21 deg C
SUBSTAGE(2) 18 hours, 20 deg C

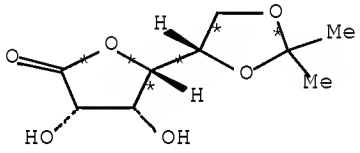
STAGE(2)
RGT L 124-41-4 NaOMe
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 35 minutes, 0 deg C
SUBSTAGE(2) 30 minutes, 0 deg C

STAGE(3)
RGT P 7664-93-9 H2SO4
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 3 hours, 0 - 5 deg C
SUBSTAGE(2) 2 hours, 0 - 2 deg C

STAGE(4)
RGT AA 298-14-6 KHCO3
SOL 7732-18-5 Water
CON 1 hour, 0 - 6 deg C, pH 7

PRO T 866594-60-7
NTE stereoselective, other diastereomer also detected, 3.75:1 diastereomeric ratio, safety, alternative prepn. also described

RX(23) OF 23 COMPOSED OF RX(7), RX(2), RX(3), RX(4), RX(5)
RX(23) 2 AB + 2 G + 2 K + 2 L ===> W



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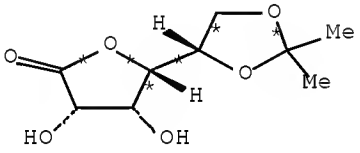
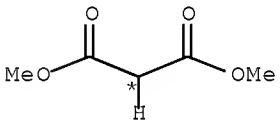


AB



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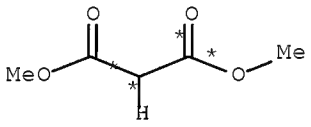

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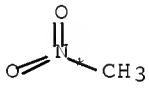
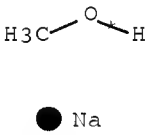
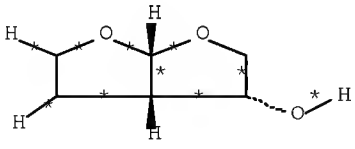


2 K



2 L

5
STEPS



W
YIELD 76%

RX(7) RCT AB 94697-68-4
RGT AC 7790-21-8 KIO4, AA 298-14-6 KHCO3
PRO A 22323-80-4

```
          SOL  7732-18-5 Water, 109-99-9 THF
          CON  SUBSTAGE(1) 3 hours, 32 - 34 deg C
               SUBSTAGE(2) 4.5 hours, 32 deg C

RX(2)     RCT  A 22323-80-4, G 108-59-8

            STAGE(1)
               SOL  109-99-9 THF
               CON  3 hours, 20 deg C

            STAGE(2)
               RGT  I 110-86-1 Pyridine
               CON  20 hours

            STAGE(3)
               RGT  J 108-24-7 Ac2O
               SOL  109-99-9 THF
               CON  SUBSTAGE(1) 4 hours, 45 deg C
                    SUBSTAGE(2) 12 hours, 45 deg C

          PRO  H 204390-79-4

RX(3)     RCT  H 204390-79-4, K 75-52-5

            STAGE(1)
               RGT  O 6674-22-2 DBU
               SOL  67-56-1 MeOH
               CON  SUBSTAGE(1) 0.5 hours, 0 - 25 deg C
                    SUBSTAGE(2) 3 hours, 20 deg C

            STAGE(2)
               RCT  L 124-41-4
               SOL  67-56-1 MeOH
               CON  30 minutes, 0 - 3 deg C

            STAGE(3)
               RGT  P 7664-93-9 H2SO4
               SOL  67-56-1 MeOH
               CON  5 hours, 0 - 3 deg C

            STAGE(4)
               RGT  Q 144-55-8 NaHCO3
               SOL  7732-18-5 Water, 141-78-6 AcOEt
               CON  0 - 15 deg C, pH 6.5 - 7

          PRO  M 874290-09-2, N 874290-10-5
          NTE  stereoselective, traces of other diastereomers also detected

RX(4)     RCT  M 874290-09-2

            STAGE(1)
               RGT  U 1310-58-3 KOH
               SOL  7732-18-5 Water, 67-56-1 MeOH
               CON  2 hours, reflux

            STAGE(2)
               RGT  V 64-19-7 AcOH
               CON  35 deg C

          PRO  T 866594-60-7
```

NTE stereoselective, alternative prepn. gave lower stereoselectivity

RX(5) RCT T 866594-60-7

STAGE(1)
RGT X 16949-15-8 LiBH4
SOL 109-99-9 THF
CON SUBSTAGE(1) 0.5 hours, room temperature
SUBSTAGE(2) 2.5 hours, 50 deg C

STAGE(2)
RGT Y 7647-01-0 HCl
SOL 7732-18-5 Water
CON SUBSTAGE(1) 4 hours, -10 - -5 deg C
SUBSTAGE(2) 2 hours, -10 deg C

STAGE(3)
RGT Z 121-44-8 Et3N
CON 1 hour, <0 deg C

PRO W 156928-09-5
NTE stereoselective
AN 144:170908 CASREACT Full-text

L71 ANSWER 3 OF 3 CASREACT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 143:367012 CASREACT Full-text
TITLE: Methods for the preparation of (3R,3aS,6aR) hexahydro-furo[2,3-b]furan-3-ol
INVENTOR(S): Quaedflieg, Peter Jan Leonard Mario; Kesteleyn, Bart Rudolf Romanie; Vijn, Robert Jan; Liebregts, Constantinus Simon Maria; Kooistra, Jacob Hermanus Matheus Hero; Lommen, Franciscus Alphons Marie
PATENT ASSIGNEE(S): Tibotec Pharmaceuticals Ltd., Ire.
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005095410	A1	20051013	WO 2005-EP51452	20050331
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005229435	A1	20051013	AU 2005-229435	20050331
CA 2559959	A1	20051013	CA 2005-2559959	20050331
EP 1732931	A1	20061220	EP 2005-729507	20050331
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HR, LV, MK, YU

CN 1938316	A	20070328	CN 2005-80010400	20050331
BR 2005009514	A	20070911	BR 2005-9514	20050331
JP 2007530638	T	20071101	JP 2007-505559	20050331
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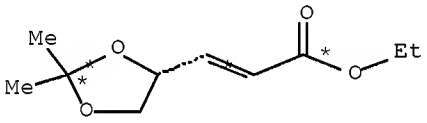
MX 2006PA11281	A	20061207	MX 2006-PA11281	20060929
US 20070208184	A1	20070906	US 2006-599497	20060929
NO 2006004977	A	20061031	NO 2006-4977	20061031
PRIORITY APPLN. INFO.:			EP 2004-101336	20040331
			WO 2005-EP51452	20050331

OTHER SOURCE(S): MARPAT 143:387012

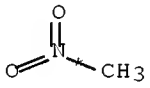
AB The present invention relates to methods for the preparation of diastereomerically pure (3R,3aS,6aR) hexahydro-furo[2,3-b]furan-3-ol (I) as well as a novel intermediate, (3aR,4S,6aS) 4-methoxy-tetrahydro- furo[3,4-b]furan-2-one (II) for use in said methods. More in particular the invention relates to a stereoselective method for the preparation of diastereomerically pure I, as well as methods for the crystallization of II and for the epimerization of (3aR,4R,6aS) 4-methoxy-tetrahydro-furo[3,4-b]- furan-2-one to II.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(3) OF 15 ...2 H + 2 J + 2 K ===> L + M



2 H



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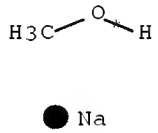

2 K

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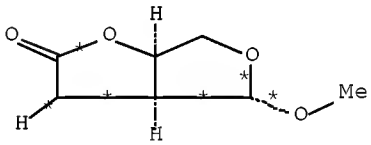
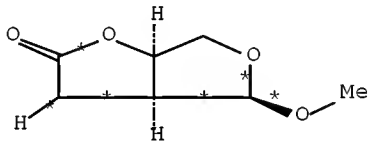


L
YIELD 53%(76)



M
YIELD 53%(24)

RX(3) RCT H 104321-62-2, J 75-52-5

STAGE(1)
SOL 67-56-1 MeOH
CON room temperature -> 0 deg C

STAGE(2)
RGT N 6674-22-2 DBU
CON SUBSTAGE(1) 25 minutes, 0 deg C
SUBSTAGE(2) 17 hours, 20 deg C

STAGE(3)
RCT K 124-41-4
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 10 minutes, 0 deg C
SUBSTAGE(2) 50 minutes, 0 deg C

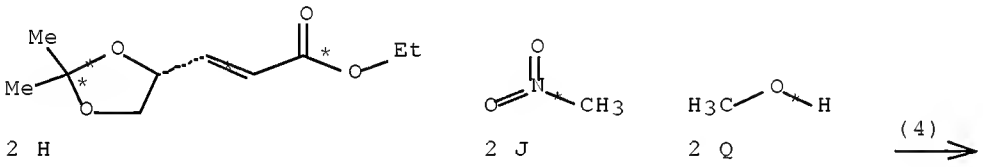
STAGE(4)
RGT O 7664-93-9 H2SO4
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 60 minutes, 0 - 5 deg C
SUBSTAGE(2) 2 hours, 0 deg C

STAGE(5)
RGT P 144-55-8 NaHCO3
SOL 7732-18-5 Water, 141-78-6 AcOEt
CON 15 minutes, 0 - 5 deg C, pH 6.9

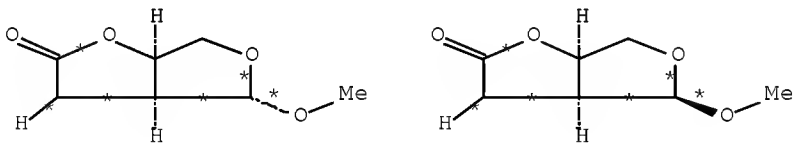
STAGE(6)
RGT O 7664-93-9 H2SO4
SOL 141-78-6 AcOEt
CON 0 - 5 deg C, pH 4.2

PRO L 866594-60-7, M 866594-61-8
NTE Michael addition, Nef reaction, stereoselective

RX(4) OF 15 ...2 H + 2 J + 2 Q ===> L + M



2 H 2 J 2 Q



L M

RX(4) RCT H 104321-62-2, J 75-52-5

STAGE(1)
SOL 67-56-1 MeOH
CON room temperature -> 0 deg C

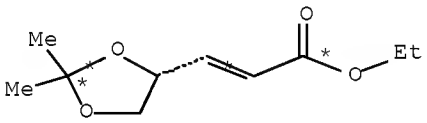
STAGE(2)
RGT N 6674-22-2 DBU
CON SUBSTAGE(1) 25 minutes, 0 deg C

SUBSTAGE(2) 17 hours, 20 deg C

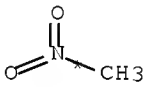
STAGE(3)
RCT Q 67-56-1
RGT O 7664-93-9 H2SO4
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 40 minutes, 0 deg C
SUBSTAGE(2) 4 hours, 0 deg C

PRO L 866594-60-7, M 866594-61-8
NTE Michael addition, Nef reaction, 35% overall yield, stereoselective

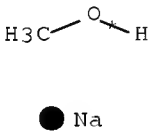
RX(5) OF 15 2 H + 2 J + 2 K ===> L + M



2 H

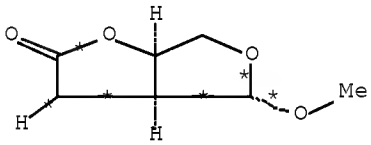


2 J

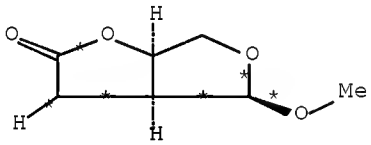


2 K

(5) →



L
YIELD 53%(73)



M
YIELD 53%(27)

RX(5) RCT H 104321-62-2, J 75-52-5

STAGE(1)
SOL 67-56-1 MeOH
CON room temperature -> 0 deg C

STAGE(2)
RGT S 80-70-6 Me2NC(:NH)NMe2
CON SUBSTAGE(1) 20 minutes, 0 deg C
SUBSTAGE(2) 22 hours, 20 deg C

STAGE(3)
RCT K 124-41-4
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 15 minutes, 0 deg C
SUBSTAGE(2) 70 minutes, 0 deg C

STAGE(4)
RGT O 7664-93-9 H2SO4

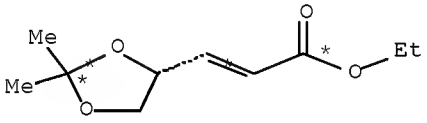
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 70 minutes, 0 - 5 deg C
SUBSTAGE(2) 145 minutes, 0 deg C

STAGE(5)
RGT P 144-55-8 NaHCO3
SOL 7732-18-5 Water, 141-78-6 AcOEt
CON 30 minutes, 0 deg C, pH 7.4

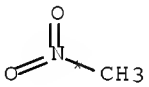
STAGE(6)
RGT O 7664-93-9 H2SO4
SOL 141-78-6 AcOEt
CON 0 deg C, pH 4.2

PRO L 866594-60-7, M 866594-61-8
NTE Michael addition, Nef reaction, stereoselective

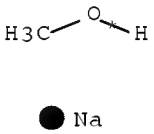
RX(6) OF 15 2 H + 2 J + 2 K ===> L + M



2 H

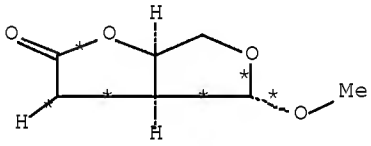


2 J

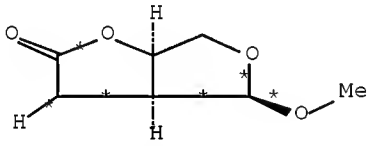


2 K

(6)



L
YIELD 42%(75)



M
YIELD 42%(25)

RX(6) RCT H 104321-62-2, J 75-52-5

STAGE(1)
SOL 67-56-1 MeOH
CON room temperature -> 0 deg C

STAGE(2)
RCT K 124-41-4
SOL 67-56-1 MeOH
CON 18 hours, 0 deg C

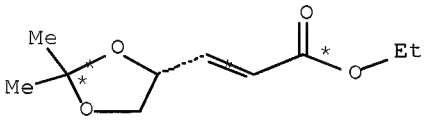
STAGE(3)
RGT O 7664-93-9 H2SO4
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 75 minutes, -3 - 0 deg C
SUBSTAGE(2) 4 hours, 0 deg C

SUBSTAGE(3) 16 hours, -30 deg C

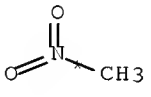
STAGE(4)
RGT P 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON 90 minutes, 0 - 5 deg C, pH 5 - 5.5

PRO L 866594-60-7, M 866594-61-8
NTE Michael addition, Nef reaction, stereoselective

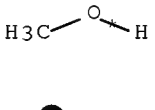
RX(7) OF 15 2 H + 2 J + 2 K ===> L + M



2 H

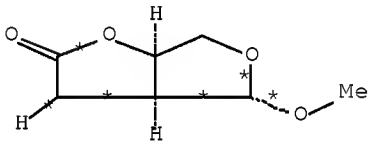


2 J

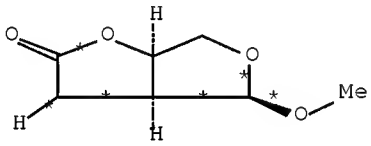


2 K

(7)



L
YIELD 31%



M
YIELD 1%

RX(7) RCT H 104321-62-2, J 75-52-5

STAGE(1)
SOL 67-56-1 MeOH
CON room temperature -> 0 deg C

STAGE(2)
RGT N 6674-22-2 DBU
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 20 minutes, 0 deg C
SUBSTAGE(2) 16.5 hours, 20 deg C

STAGE(3)
RCT K 124-41-4
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 20 minutes, 0 deg C
SUBSTAGE(2) 50 minutes, 0 deg C

STAGE(4)
RGT O 7664-93-9 H2SO4
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 0 - 5 deg C

SUBSTAGE(2) 2 hours, 0 - 2 deg C

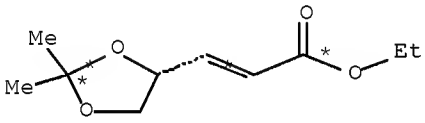
STAGE(5)
RGT P 144-55-8 NaHCO3
SOL 7732-18-5 Water, 141-78-6 AcOEt
CON 17 minutes, 0 - 9 deg C, pH 7.2

STAGE(6)
RGT O 7664-93-9 H2SO4
SOL 67-56-1 MeOH
CON 9 deg C, pH 4

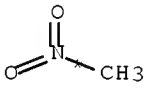
STAGE(7)
SOL 67-63-0 Me2CHOH
CON SUBSTAGE(1) 80 deg C
SUBSTAGE(2) 80 deg C -> 60 deg C
SUBSTAGE(3) 2 hours, 60 deg C -> 0 deg C

PRO L 866594-60-7, M 866594-61-8
NTE Michael addition, Nef reaction, alternate prepn. shown, stereoselective

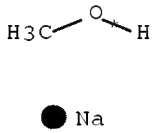
RX(8) OF 15 ...H + J + K ===> L



H

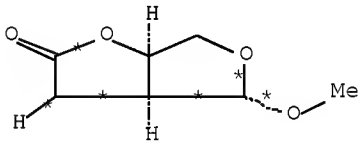


J



K

(8) →



L
YIELD 51%

RX(8) RCT H 104321-62-2, J 75-52-5

STAGE(1)
SOL 67-56-1 MeOH
CON room temperature -> 0 deg C

STAGE(2)
RGT N 6674-22-2 DBU
CON SUBSTAGE(1) 50 minutes, 0 - 5 deg C
SUBSTAGE(2) 16 hours, 20 deg C

STAGE(3)
RCT K 124-41-4
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 50 minutes, 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C

STAGE(4)
RGT O 7664-93-9 H2SO4
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 3 hours, 0 - 5 deg C
SUBSTAGE(2) 2 hours, 0 - 5 deg C

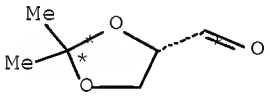
STAGE(5)
RGT D 298-14-6 KHCO3
SOL 7732-18-5 Water
CON 1 hour, 0 - 5 deg C, pH 3.5

STAGE(6)
RGT U 75-75-2 MeSO3H
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 2 hours, 50 deg C
SUBSTAGE(2) 12 hours, 20 deg C

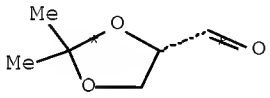
STAGE(7)
RGT V 121-44-8 Et3N
CON 2 hours, -5 deg C

PRO L 866594-60-7
NTE Michael addition, Nef reaction, alternate prepn. shown, stereoselective

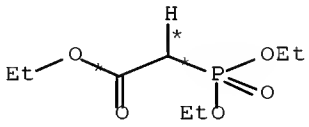
RX(10) OF 15 COMPOSED OF RX(2), RX(3)
RX(10) 2 B + 2 G + 2 J + 2 K ===> L + M



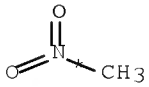
B



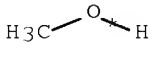
B



2 G

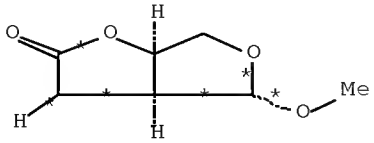


2 J

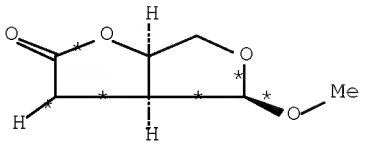


2 K

2
STEPS



L
YIELD 53%(76)



M
YIELD 53%(24)

RX(2) RCT B 22323-80-4, G 867-13-0

STAGE(1)
CON 25 minutes, 13 - 17 deg C

STAGE(2)
RGT I 584-08-7 K2CO3
CON SUBSTAGE(1) 30 minutes, 17 - 25 deg C, pH 11.6
SUBSTAGE(2) 17 hours, 20 deg C, pH 11.6

PRO H 104321-62-2
NTE stereoselective

RX(3) RCT H 104321-62-2, J 75-52-5

STAGE(1)
SOL 67-56-1 MeOH
CON room temperature -> 0 deg C

STAGE(2)
RGT N 6674-22-2 DBU
CON SUBSTAGE(1) 25 minutes, 0 deg C
SUBSTAGE(2) 17 hours, 20 deg C

STAGE(3)
RCT K 124-41-4
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 10 minutes, 0 deg C
SUBSTAGE(2) 50 minutes, 0 deg C

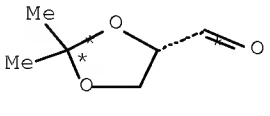
STAGE(4)
RGT O 7664-93-9 H2SO4
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 60 minutes, 0 - 5 deg C
SUBSTAGE(2) 2 hours, 0 deg C

STAGE(5)
RGT P 144-55-8 NaHCO3
SOL 7732-18-5 Water, 141-78-6 AcOEt
CON 15 minutes, 0 - 5 deg C, pH 6.9

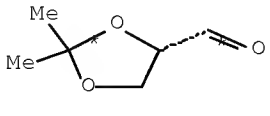
STAGE(6)
RGT O 7664-93-9 H2SO4
SOL 141-78-6 AcOEt
CON 0 - 5 deg C, pH 4.2

PRO L 866594-60-7, M 866594-61-8
NTE Michael addition, Nef reaction, stereoselective

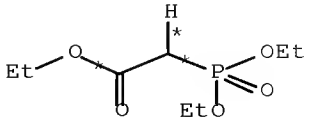
RX(11) OF 15 COMPOSED OF RX(2), RX(4)
RX(11) 2 B + 2 G + 2 J + 2 Q ===> L + M



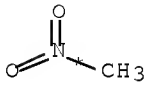
B



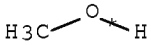
B



2 G

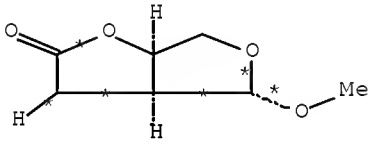


2 J

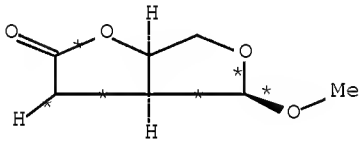


2 Q

2 STEPS



L



M

RX(2) RCT B 22323-80-4, G 867-13-0

STAGE(1)
CON 25 minutes, 13 - 17 deg C

STAGE(2)
RGT I 584-08-7 K2CO3
CON SUBSTAGE(1) 30 minutes, 17 - 25 deg C, pH 11.6
SUBSTAGE(2) 17 hours, 20 deg C, pH 11.6

PRO H 104321-62-2
NTE stereoselective

RX(4) RCT H 104321-62-2, J 75-52-5

STAGE(1)
SOL 67-56-1 MeOH

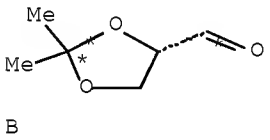
CON room temperature -> 0 deg C

STAGE(2)
RGT N 6674-22-2 DBU
CON SUBSTAGE(1) 25 minutes, 0 deg C
SUBSTAGE(2) 17 hours, 20 deg C

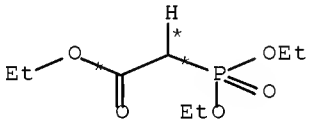
STAGE(3)
RCT Q 67-56-1
RGT O 7664-93-9 H2SO4
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 40 minutes, 0 deg C
SUBSTAGE(2) 4 hours, 0 deg C

PRO L 866594-60-7, M 866594-61-8
NTE Michael addition, Nef reaction, 35% overall yield, stereoselective

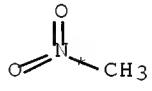
RX(12) OF 15 COMPOSED OF RX(2), RX(8)
RX(12) B + G + J + K ===> L



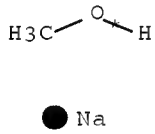
B



G

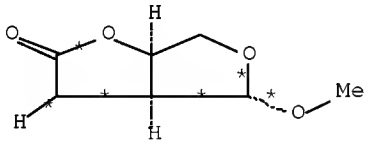


J



K

2 STEPS



L
YIELD 51%

RX(2) RCT B 22323-80-4, G 867-13-0

STAGE(1)
CON 25 minutes, 13 - 17 deg C

STAGE(2)
RGT I 584-08-7 K2CO3
CON SUBSTAGE(1) 30 minutes, 17 - 25 deg C, pH 11.6
SUBSTAGE(2) 17 hours, 20 deg C, pH 11.6

PRO H 104321-62-2
NTE stereoselective

RX(8) RCT H 104321-62-2, J 75-52-5

STAGE(1)
SOL 67-56-1 MeOH
CON room temperature -> 0 deg C

STAGE(2)
RGT N 6674-22-2 DBU
CON SUBSTAGE(1) 50 minutes, 0 - 5 deg C
SUBSTAGE(2) 16 hours, 20 deg C

STAGE(3)
RCT K 124-41-4
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 50 minutes, 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C

STAGE(4)
RGT O 7664-93-9 H2SO4
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 3 hours, 0 - 5 deg C
SUBSTAGE(2) 2 hours, 0 - 5 deg C

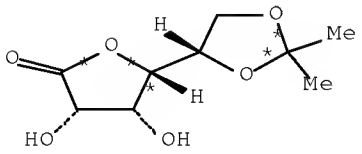
STAGE(5)
RGT D 298-14-6 KHCO3
SOL 7732-18-5 Water
CON 1 hour, 0 - 5 deg C, pH 3.5

STAGE(6)
RGT U 75-75-2 MeSO3H
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 2 hours, 50 deg C
SUBSTAGE(2) 12 hours, 20 deg C

STAGE(7)
RGT V 121-44-8 Et3N
CON 2 hours, -5 deg C

PRO L 866594-60-7
NTE Michael addition, Nef reaction, alternate prepn. shown, stereoselective

RX(13) OF 15 COMPOSED OF RX(1), RX(2), RX(3)
RX(13) 2 A + 2 G + 2 J + 2 K ===> L + M



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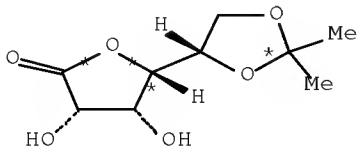

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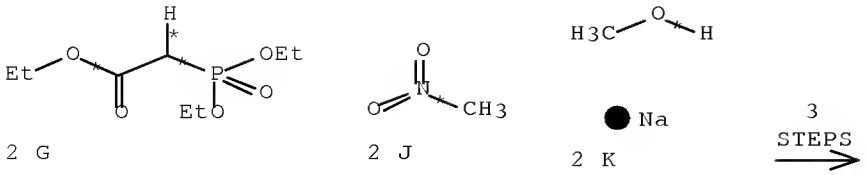
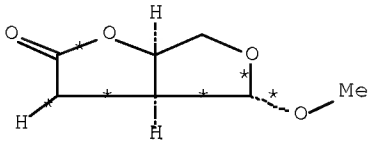
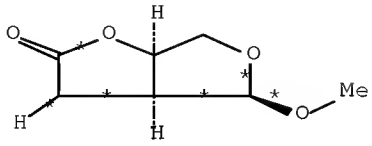




L
YIELD 53%(76)



M
YIELD 53%(24)

RX(1) RCT A 94697-68-4
RGT C 7790-21-8 KIO4, D 298-14-6 KHCO3
PRO B 22323-80-4
SOL 7732-18-5 Water, 109-99-9 THF
CON SUBSTAGE(1) 3 hours, 32 - 34 deg C
SUBSTAGE(2) 4.5 hours, 32 deg C
SUBSTAGE(3) 14 hours, 5 deg C

RX(2) RCT B 22323-80-4, G 867-13-0

STAGE(1)
CON 25 minutes, 13 - 17 deg C

STAGE(2)
RGT I 584-08-7 K2CO3
CON SUBSTAGE(1) 30 minutes, 17 - 25 deg C, pH 11.6
SUBSTAGE(2) 17 hours, 20 deg C, pH 11.6

PRO H 104321-62-2
NTE stereoselective

RX(3) RCT H 104321-62-2, J 75-52-5

STAGE(1)
SOL 67-56-1 MeOH
CON room temperature -> 0 deg C

STAGE(2)
RGT N 6674-22-2 DBU
CON SUBSTAGE(1) 25 minutes, 0 deg C
SUBSTAGE(2) 17 hours, 20 deg C

STAGE(3)
RCT K 124-41-4
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 10 minutes, 0 deg C

SUBSTAGE(2) 50 minutes, 0 deg C

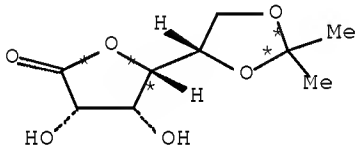
STAGE(4)
RGT O 7664-93-9 H2SO4
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 60 minutes, 0 - 5 deg C
SUBSTAGE(2) 2 hours, 0 deg C

STAGE(5)
RGT P 144-55-8 NaHCO3
SOL 7732-18-5 Water, 141-78-6 AcOEt
CON 15 minutes, 0 - 5 deg C, pH 6.9

STAGE(6)
RGT O 7664-93-9 H2SO4
SOL 141-78-6 AcOEt
CON 0 - 5 deg C, pH 4.2

PRO L 866594-60-7, M 866594-61-8
NTE Michael addition, Nef reaction, stereoselective

RX(14) OF 15 COMPOSED OF RX(1), RX(2), RX(4)
RX(14) 2 A + 2 G + 2 J + 2 Q ===> L + M



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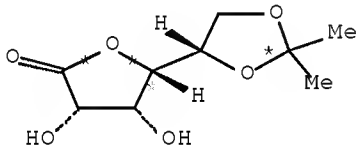

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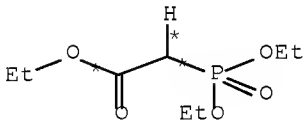
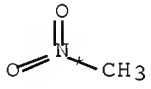
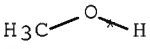


2 G

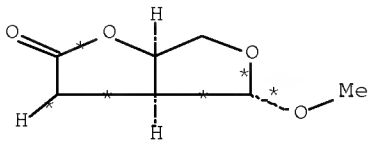


2 J



2 Q

3
STEPS



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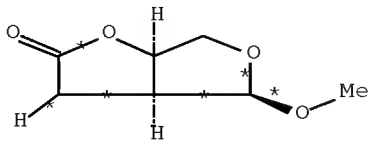


M

RX(1) RCT A 94697-68-4
RGT C 7790-21-8 KIO4, D 298-14-6 KHCO3
PRO B 22323-80-4
SOL 7732-18-5 Water, 109-99-9 THF
CON SUBSTAGE(1) 3 hours, 32 - 34 deg C
SUBSTAGE(2) 4.5 hours, 32 deg C
SUBSTAGE(3) 14 hours, 5 deg C

RX(2) RCT B 22323-80-4, G 867-13-0

STAGE(1)
CON 25 minutes, 13 - 17 deg C

STAGE(2)
RGT I 584-08-7 K2CO3
CON SUBSTAGE(1) 30 minutes, 17 - 25 deg C, pH 11.6
SUBSTAGE(2) 17 hours, 20 deg C, pH 11.6

PRO H 104321-62-2
NTE stereoselective

RX(4) RCT H 104321-62-2, J 75-52-5

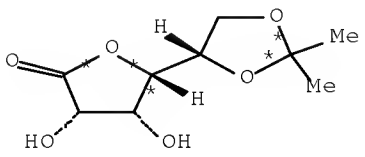
STAGE(1)
SOL 67-56-1 MeOH
CON room temperature -> 0 deg C

STAGE(2)
RGT N 6674-22-2 DBU
CON SUBSTAGE(1) 25 minutes, 0 deg C
SUBSTAGE(2) 17 hours, 20 deg C

STAGE(3)
RCT Q 67-56-1
RGT O 7664-93-9 H2SO4
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 40 minutes, 0 deg C
SUBSTAGE(2) 4 hours, 0 deg C

PRO L 866594-60-7, M 866594-61-8
NTE Michael addition, Nef reaction, 35% overall yield, stereoselective

RX(15) OF 15 COMPOSED OF RX(1), RX(2), RX(8)
RX(15) A + G + J + K ===> L



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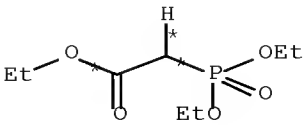

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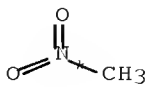
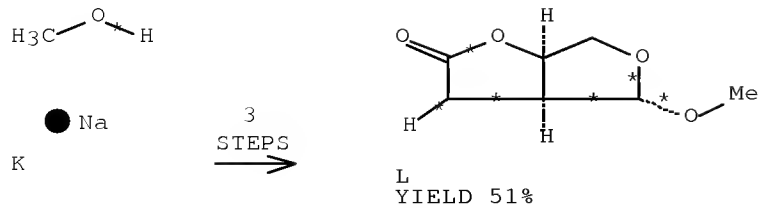


J



L
YIELD 51%

RX(1) RCT A 94697-68-4
RGT C 7790-21-8 KIO4, D 298-14-6 KHCO3
PRO B 22323-80-4
SOL 7732-18-5 Water, 109-99-9 THF
CON SUBSTAGE(1) 3 hours, 32 - 34 deg C
SUBSTAGE(2) 4.5 hours, 32 deg C
SUBSTAGE(3) 14 hours, 5 deg C

RX(2) RCT B 22323-80-4, G 867-13-0

STAGE(1)
CON 25 minutes, 13 - 17 deg C

STAGE(2)
RGT I 584-08-7 K2CO3
CON SUBSTAGE(1) 30 minutes, 17 - 25 deg C, pH 11.6
SUBSTAGE(2) 17 hours, 20 deg C, pH 11.6

PRO H 104321-62-2
NTE stereoselective

RX(8) RCT H 104321-62-2, J 75-52-5

STAGE(1)
SOL 67-56-1 MeOH
CON room temperature -> 0 deg C

STAGE(2)
RGT N 6674-22-2 DBU
CON SUBSTAGE(1) 50 minutes, 0 - 5 deg C
SUBSTAGE(2) 16 hours, 20 deg C

STAGE(3)
RCT K 124-41-4
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 50 minutes, 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C

STAGE(4)
RGT O 7664-93-9 H2SO4
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 3 hours, 0 - 5 deg C
SUBSTAGE(2) 2 hours, 0 - 5 deg C

STAGE(5)

RGT D 298-14-6 KHCO3
SOL 7732-18-5 Water
CON 1 hour, 0 - 5 deg C, pH 3.5

STAGE(6)
RGT U 75-75-2 MeSO3H
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 2 hours, 50 deg C
SUBSTAGE(2) 12 hours, 20 deg C

STAGE(7)
RGT V 121-44-8 Et3N
CON 2 hours, -5 deg C

PRO L 866594-60-7
NTE Michael addition, Nef reaction, alternate prepn. shown, stereoselective
AN 143:387012 CASREACT Full-text

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DICTIONARY FILE UPDATES:   2 JUN 2008  HIGHEST RN 1024742-83-3

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FILE COVERS 1907 - 3 Jun 2008  VOL 148 ISS 23
FILE LAST UPDATED: 2 Jun 2008  (20080602/ED)

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'OBI' IS DEFAULT SEARCH FIELD FOR 'ZCAPLUS' FILE

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                6674-22-2/BI OR 67-63-0/BI OR 75-52-5/BI OR 75-65-0/BI OR
                75-75-2/BI OR 75-85-4/BI OR 80-70-6/BI OR 865-34-9/BI OR
                866594-60-7/BI OR 866594-61-8/BI OR 867-13-0/BI OR 94697-68-4/B
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L5              4 SEA FILE=REGISTRY ABB=ON  PLU=ON  L3 AND L4
L6           1642 SEA FILE=REGISTRY ABB=ON  PLU=ON  C6H10O3/MF
L7             22 SEA FILE=REGISTRY ABB=ON  PLU=ON  L6 AND L4
L10            20 SEA FILE=REGISTRY ABB=ON  PLU=ON  "FURO(2,3-B)FURAN-3-OL,
                  HEXAHYDRO-"?/CN
L12             7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L7 AND L10
L14            43 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L12
L16             3 SEA FILE=REGISTRY ABB=ON  PLU=ON  L5 NOT L12
L20             5 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L16
L21             3 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L14 AND L20


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                  75-75-2/BI OR 75-85-4/BI OR 80-70-6/BI OR 865-34-9/BI OR
                  866594-60-7/BI OR 866594-61-8/BI OR 867-13-0/BI OR 94697-68-4/B
                  I)
L4          84397 SEA FILE=REGISTRY ABB=ON  PLU=ON  2 OC4/ESS
L5              4 SEA FILE=REGISTRY ABB=ON  PLU=ON  L3 AND L4
L6           1642 SEA FILE=REGISTRY ABB=ON  PLU=ON  C6H10O3/MF
L7             22 SEA FILE=REGISTRY ABB=ON  PLU=ON  L6 AND L4
L10            20 SEA FILE=REGISTRY ABB=ON  PLU=ON  "FURO(2,3-B)FURAN-3-OL,
                  HEXAHYDRO-"?/CN
L12             7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L7 AND L10
L14            43 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L12
L16             3 SEA FILE=REGISTRY ABB=ON  PLU=ON  L5 NOT L12
L20             5 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L16
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                  501921-23-9/BI OR 501921-24-0/BI OR 501921-25-1/BI OR 501921-26
                  -2/BI OR 501921-27-3/BI OR 501921-28-4/BI OR 501921-29-5/BI OR
                  501921-31-9/BI OR 501921-32-0/BI OR 6674-22-2/BI OR 67-63-0/BI
                  OR 75-52-5/BI OR 75-65-0/BI OR 75-75-2/BI OR 75-85-4/BI OR
                  80-70-6/BI OR 865-34-9/BI OR 866594-61-8/BI OR 874290-09-2/BI
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=> d stat que L39
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L6           1642 SEA FILE=REGISTRY ABB=ON  PLU=ON  C6H10O3/MF
L7             22 SEA FILE=REGISTRY ABB=ON  PLU=ON  L6 AND L4
L10            20 SEA FILE=REGISTRY ABB=ON  PLU=ON  "FURO(2,3-B)FURAN-3-OL,
                  HEXAHYDRO-"?/CN
L12             7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L7 AND L10
L14            43 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L12
L23       1933411 SEA FILE=REGISTRY ABB=ON  PLU=ON  ?NITRO?/CNS
L33               TRANSFER  PLU=ON  L14 1- RN :    3468 TERMS
L34          3468 SEA FILE=REGISTRY ABB=ON  PLU=ON  L33
L35           102 SEA FILE=REGISTRY ABB=ON  PLU=ON  L34 AND L23
L36            50 SEA FILE=REGISTRY ABB=ON  PLU=ON  L35 AND ?NITROPHENYL?/CNS
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L37          52 SEA FILE=REGISTRY ABB=ON  PLU=ON  L35 NOT L36
L38           4 SEA FILE=REGISTRY ABB=ON  PLU=ON  L37 AND ?NITROMETHYL?/CNS
L39           2 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L38 AND L14


=> s (L21 or L25 or L39) not L72
L73           1 (L21 OR L25 OR L39) NOT L72

=> file casreact
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FILE CONTENT:1840 - 31 May 2008 VOL 148 ISS 23

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                75-75-2/BI OR 75-85-4/BI OR 80-70-6/BI OR 865-34-9/BI OR
                866594-60-7/BI OR 866594-61-8/BI OR 867-13-0/BI OR 94697-68-4/B
                I)
L4         84397 SEA FILE=REGISTRY ABB=ON  PLU=ON  2 OC4/ESS
L5             4 SEA FILE=REGISTRY ABB=ON  PLU=ON  L3 AND L4
L6          1642 SEA FILE=REGISTRY ABB=ON  PLU=ON  C6H10O3/MF
L7            22 SEA FILE=REGISTRY ABB=ON  PLU=ON  L6 AND L4
L10           20 SEA FILE=REGISTRY ABB=ON  PLU=ON  "FURO(2,3-B)FURAN-3-OL,
                HEXAHYDRO-"?/CN
L12            7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L7 AND L10
L16            3 SEA FILE=REGISTRY ABB=ON  PLU=ON  L5 NOT L12
L40           18 SEA FILE=CASREACT ABB=ON  PLU=ON  L12
L41            3 SEA FILE=CASREACT ABB=ON  PLU=ON  L16
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=> d stat que L48
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L6          1642 SEA FILE=REGISTRY ABB=ON  PLU=ON  C6H10O3/MF
L7            22 SEA FILE=REGISTRY ABB=ON  PLU=ON  L6 AND L4
L10           20 SEA FILE=REGISTRY ABB=ON  PLU=ON  "FURO(2,3-B)FURAN-3-OL,
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L40            18 SEA FILE=CASREACT ABB=ON  PLU=ON  L12
L47          4646 SEA FILE=CASREACT ABB=ON  PLU=ON  75-52-5
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=> s (L42 or L48) not L71
L74             0 (L42 OR L48) NOT L71

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L74 HAS NO ANSWERS
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FILE LAST UPDATED: 2 Jun 2008  (20080602/ED)

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'OBI' IS DEFAULT SEARCH FIELD FOR 'ZCAPLUS' FILE
PROCESSING COMPLETED FOR L73
PROCESSING COMPLETED FOR L74
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                  ANSWER '1' FROM FILE ZCAPLUS

=> d ibib abs hitind hitstr L75 1

L75  ANSWER 1 OF 1  ZCAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2007:226929  ZCAPLUS  Full-text
DOCUMENT NUMBER:          146:296223
TITLE:                    Preparation of spiroisoxazoline-based peptidomimetics
                          as inhibitors of serine proteases, particularly HCV
                          NS3-NS4A protease
INVENTOR(S):              Cottrell, Kevin M.; Maxwell, John; Tang, Qing;
                          Grillot, Anne-Laure; Le Tiran, Arnaud; Perola,
                          Emanuele
PATENT ASSIGNEE(S):       Vertex Pharmaceuticals Incorporated, USA
SOURCE:                   PCT Int. Appl., 489pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:
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PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2007025307	A2	20070301	WO 2006-US33770		20060828
WO 2007025307	A3	20070426			

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

AU 2006282771	A1	20070301	AU 2006-282771		20060828
CA 2620621	A1	20070301	CA 2006-2620621		20060828
US 20070179167	A1	20070802	US 2006-511109		20060828
EP 1917269	A2	20080507	EP 2006-813916		20060828

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS

IN 2008MN00446	A	20080404	IN 2008-MN446		20080310
KR 2008041715	A	20080513	KR 2008-707149		20080325
PRIORITY APPLN. INFO.:			US 2005-711530P	P	20050826
			WO 2006-US33770	W	20060828

OTHER SOURCE(S): MARPAT 146:296223

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to spiroisoxazoline-based peptidomimetics I [A = (CX1X2)a; B = (CX1X2)b; X1, X2 = independently H, halo, NH2, sulfanyl, (un)substituted aryl, etc.; or CX1X2 = C(:O); R1 = -ZAR4; ZA = a bond, (un)substituted aliphatic chain wherein up to 3 C units of ZA are optionally and independently replaced by CO, CS, CONH and derivs., S, SO, etc.; R4 = H, OH, halo, CN, (un)substituted hetero/aryl, etc.; R2 = -ZBR5; ZB = independently a bond or (un)substituted aliphatic chain wherein up to 3 C units of ZA are optionally and independently replaced by CO, CS, CONH and derivs., SO2NH and derivs., COO, etc.; R5 = halo, OCF3, NH2, (un)substituted aryl, etc.; or R1NCCR2 = (un)substituted heterocycloaliph. ring; R3 = NH2, S, SO, SO2, aryl, etc.; Y, Y' = independently -ZDR7; ZD = a bond, (un)substituted aliphatic chain wherein up to 2 C units of ZA are optionally and independently replaced by CO, CS, CONH and derivs., NHSO2 and derivs., etc.; or CYY' = C(:O), C(:S); R7 = H, halo, OH, CN, NO2, NH2, OCF3, (un)substituted aryl; a, b = independently 0-3; provided that a+b = 2-3; with provisos] or their pharmaceutically acceptable salts or mixts. that inhibit serine protease activity, particularly the activity of hepatitis C virus (HCV) NS3-NS4A protease. Thus, a multi-step synthesis using 4-methoxy-3,5-dimethylbenzaldehyde, (S)-di-tert-Bu 4-methylenepyrrolidine-1,2-dicarboxylate, N-(tert-butoxycarbonyl)-L-tert- butylglycine, cyclohexaneacetic acid and (3S)-3-amino-N-cyclopropyl-2- hydroxyhexanamde gave spiroisoxazoline II. Selected I exhibited Ki values ranging from about 0.008 to about 0.100 μM in an HCV assay.

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 7, 63

IT 60-12-8, 2-Phenylethanol 78-81-9, Isobutylamine 85-46-1, 1-Naphthylsulfonyl chloride 86-84-0, 1-Naphthyl isocyanate 98-89-5, Cyclohexanecarboxylic acid 98-97-5, 2-Pyrazinecarboxylic acid 100-55-0, 3-Pyridinemethanol 100-72-1 102-56-7, 2,5-Dimethoxyaniline 103-71-9, Phenyl isocyanate, reactions 105-36-2, Ethyl bromoacetate 107-10-8, Propylamine, reactions 108-03-2, 1-Nitropropane 108-23-6, Isopropyl chloroformate 108-30-5, Succinic anhydride, reactions 109-85-3, 2-Methoxyethylamine 109-89-7, N,N-Diethylamine, reactions 109-90-0, Ethyl isocyanate 123-76-2, 4-Oxopentanoic acid 368-83-2, 3-Trifluoromethylbenzaldehyde oxime 406-34-8, 2-Fluoroethylamine 443-33-4, 2-Chloro-6-fluorobenzaldehyde oxime 446-51-5, (2-Fluorophenyl)methanol 456-47-3, (3-Fluorophenyl)methanol 458-02-6, 3-Fluorobenzaldoxime 459-23-4, 4-Fluorobenzaldehyde oxime 459-31-4, 3-(4-Fluorophenyl)propanoic acid 462-27-1, 2-Fluoroethyl chloroformate 498-62-4, 3-Thiophenecarboxaldehyde 500-22-1, 3-Pyridinecarboxaldehyde 501-53-1, Benzyl chloroformate 501-81-5, 2-(Pyridin-3-yl)acetic acid 503-74-2, 3-Methylbutanoic acid 541-41-3, Ethyl chloroformate 556-97-8 586-95-8, 4-Pyridinemethanol 586-98-1, 2-Pyridinemethanol 587-03-1, m-Tolylmethanol 589-18-4, p-Tolylmethanol 608-07-1, 5-Methoxytryptamine 614-21-1, Benzoylnitromethane 616-24-0, 1-Ethylpropylamine 617-89-0, Furfurylamine 624-78-2, N-Methylethylamine 627-05-4 627-35-0, N-Methyl-N-propylamine 628-12-6, 2-Methoxyethyl chloroformate 634-97-9, 1H-Pyrrole-2-carboxylic acid 644-36-0, 2-(o-Tolyl)acetic acid 656-42-8, 2,2-Difluoro-1,3-benzodioxole-5-carboxaldehyde 696-54-8, Pyridine-4-aldoxime 699-06-9, 4-Hydroxybenzaldehyde oxime 765-30-0, Cyclopropylamine 872-53-7, Cyclopentanecarboxaldehyde 873-69-8 932-90-1 939-90-2 1003-03-8, Cyclopentylamine 1004-36-0, 2,6-Dimethyl-γ-pyrone 1007-01-8, Bicyclo[2.2.1]heptane-2-acetic acid 1070-83-3, tert-Butylacetic acid 1071-73-4, 5-Hydroxypentan-2-one 1099-45-2, (Carbethoxymethylene)triphenylphosphorane 1121-47-7, 2-Furanaldoxime 1123-00-8, Cyclopentylacetic acid 1129-37-9, 4-Nitrobenzaldehyde oxime 1188-21-2, N-Acetyl-L-leucine 1193-92-6 1552-92-7 1571-08-0, Methyl 4-formylbenzoate 1609-86-5, tert-Butyl isocyanate 1750-42-1, 3-Aminoisoxazole 1795-48-8, Isopropyl isocyanate 1798-09-0, 2-(3-Methoxyphenyl)acetic acid 1836-62-0 1899-24-7, 5-Bromo-2-furaldehyde 2039-67-0, 2-(3-Methoxyphenyl)ethylamine 2043-61-0, Cyclohexanecarboxaldehyde 2081-44-9 2089-36-3, Piperonal oxime 2169-98-4, 3,4-Dimethoxybenzaldehyde oxime 2233-18-3, 4-Hydroxy-3,5-dimethylbenzaldehyde 2237-30-1, 3-Cyanoaniline 2398-37-0, 1-Bromo-3-methoxybenzene 2516-34-9, Cyclobutylamine 2516-47-4, (Cyclopropylmethyl)amine 2627-86-3 2859-67-8, 3-(Pyridin-3-yl)propan-1-ol 2859-68-9, 3-(Pyridin-2-yl)propan-1-ol 2937-50-0, Allyl chloroformate 2975-41-9, 2-Aminoindane 3173-53-3, Cyclohexyl isocyanate 3173-56-6, Benzyl isocyanate 3235-02-7, 4-Methylbenzaldehyde oxime 3235-04-9, 4-Methoxybenzaldehyde oxime 3260-44-4 3431-62-7, 3-Nitrobenzaldehyde oxime 3471-10-1 3477-93-8, 4-Carboxybenzaldehyde oxime 3527-63-7 3544-24-9, 3-Aminobenzamide 3610-36-4, 6-Methoxytryptamine 3637-61-4, Cyclopentylmethanol 3717-28-0, 2-Chlorobenzaldehyde oxime 3724-19-4, 3-(Pyridin-3-yl)propanoic acid 3731-53-1, 4-(Aminomethyl)pyridine 3848-36-0, 4-Chlorobenzaldehyde oxime 3863-11-4, 3,4-Difluoroaniline 3886-69-9 3966-30-1 4315-07-5 4401-20-1, Cycloheptaneacetic acid 4415-82-1, Cyclobutylmethanol 4442-59-5 4628-39-1 4709-59-5 4746-97-8, 1,4-Dioxaspiro[4.5]decan-8-one 4747-72-2, Cyclopropyl isocyanate 5292-21-7, Cyclohexylacetic acid 5331-92-0, 3,4-Dichlorobenzaldehyde oxime 5337-03-1 5402-55-1, 2-(Thiophen-2-yl)ethanol 5470-95-1, 2,3-Dimethoxybenzaldehyde oxime 5603-19-0 5624-26-0 5680-79-5 5805-57-2, 1H-Benzimidazole-2-methanamine 5874-58-8, N-Benzoyl-L-proline 6125-24-2 6338-70-1 6540-33-6, Cyclobutaneacetic acid 6626-07-9

6914-74-5 6971-51-3, (3-Methoxyphenyl)methanol 6974-12-5,
1,4-Dibromo-2-butene 7051-34-5, Cyclopropylmethyl bromide 7202-43-9
7254-19-5, 5-Bromoindole-2-carboxylic acid 7478-88-8 7589-27-7,
2-(4-Fluorophenyl)ethanol 7693-46-1, 4-Nitrophenyl chloroformate
13013-02-0, Methyl 4-nitrobutyrate 13250-12-9 13268-51-4 13372-80-0,
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3-Thiopheneethanol 14345-95-0 14352-58-0 14367-54-5,
(S)-2-Methyl-3-phenylpropanoic acid 15268-31-2, 3-Pyridinyl isocyanate
15833-61-1, (Tetrahydrofuran-3-yl)methanol 18004-57-4, 9-Anthraldehyde
oxime 18364-47-1 19752-84-2 19764-32-0, N-Acetyl-D-tyrosine
19840-99-4 20173-24-4, 3-Pyridineethanamine 20859-02-3,
(S)-tert-Butylglycine 21282-10-0 24424-99-5, Di-tert-butyl dicarbonate
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28920-43-6, Fmoc-Cl 29203-59-6 29656-53-9, Pipecoline 29668-44-8,
1,4-Benzodioxan-6-carboxaldehyde 29943-42-8 30411-85-9,
N-Acetyl-D-ethionine 31874-34-7, 2,4-Dimethoxybenzaldehyde oxime
32605-62-2, 3-Bromobenzaldehyde oxime 33301-41-6 34158-71-9
34272-65-6 34967-24-3, (3,5-Dimethoxyphenyl)methanamine 35700-40-4,
2,3-Dihydrobenzofuran-7-carboxylic acid 37045-73-1 38489-80-4,
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dimethylbenzaldehyde 39545-31-8, 2-Chlorobenzyl chloroformate
39930-11-5 41049-53-0, 1-Phenylcyclopropylamine 41864-05-5
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Benzothiazolemethanamine 42466-50-2, 3-Thiophenecarboxaldoxime
50670-64-9, 3-Cyano-4-methylaniline 51163-24-7, Cyclohexanemethyl
isocyanate 52178-50-4, Methyl 3-formylbenzoate 53977-47-2
55581-61-8, 2-Methylbenzofuran-3-carboxaldehyde 55745-70-5 56137-52-1
56826-61-0, (2-Methylpyridin-3-yl)methanol 58555-21-8 60712-47-2
60716-71-4 61096-94-4, 4-Ethoxybenzaldoxime 61370-75-0,
2,2-Dimethylchromane-6-carboxaldehyde 61946-88-1, 4-Ethylbenzaldoxime
62119-81-7, 1-(Thiophen-2-yl)propan-2-ol 63071-10-3 64847-76-3,
3-Cyanobenzaldoxime 64847-77-4, 4-Cyanobenzaldehyde oxime 66046-34-2,
4-Trifluoromethylbenzaldehyde oxime 66046-42-2 67266-14-2 68030-19-3
68377-65-1 70601-62-6 70918-53-5 72784-43-1 73873-59-3,
cis-4-Methoxycyclohexanecarboxylic acid 73873-61-7, trans-4-
Methoxycyclohexanecarboxylic acid 74467-06-4 75601-36-4,
3,5-Dimethylbenzaldehyde oxime 75853-20-2 77128-72-4 78603-91-5
79538-20-8, (3,5-Difluorophenyl)methanol 82477-68-7 82796-69-8
84025-81-0 84308-24-7 85064-61-5 87341-50-2 88196-70-7
88210-96-2 90609-89-5 92501-74-1 92960-68-4 93033-57-9
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RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of spiroisoxazoline-based peptidomimetics as inhibitors of serine proteases, particularly HCV NS3-NS4A protease)

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150162-39-3 154743-01-8 156928-09-5 161321-36-4
162279-48-3 165736-03-8 175136-92-2 175204-81-6,
4-Chloro-1-methyl-1H-pyrazole-3-carboxaldehyde 175277-35-7 177966-60-8
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213982-71-9 213982-76-4 220394-91-2, Benzyl 4-isocyanatopiperidine-1-
carboxylate 233276-38-5 238743-36-7, 3,4,5-Trifluorobenzaldoxime
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3-Chloro-2-fluorobenzaldehyde oxime 892285-46-0 909772-06-1
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928064-62-4 928064-63-5 928064-64-6 928064-65-7 928064-66-8
928064-67-9 928064-68-0 928064-69-1 928064-70-4 928064-73-7
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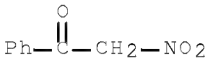
928064-85-1 928156-61-0 928156-62-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of spiroisoxazoline-based peptidomimetics as inhibitors of serine proteases, particularly HCV NS3-NS4A protease)

IT 614-21-1, Benzoylnitromethane 156928-09-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of spiroisoxazoline-based peptidomimetics as inhibitors of serine proteases, particularly HCV NS3-NS4A protease)

RN 614-21-1 ZCAPLUS
CN Ethanone, 2-nitro-1-phenyl- (CA INDEX NAME)



RN 156928-09-5 ZCAPLUS
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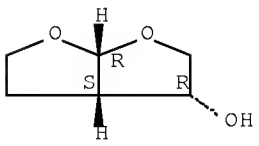
Absolute stereochemistry. Rotation (-).



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FILE LAST UPDATED: 2 Jun 2008 (20080602/ED)

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L6 1642 SEA FILE=REGISTRY ABB=ON PLU=ON C6H10O3/MF

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L76           30 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L12 (L) PREP/RL


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L78          26 L76 NOT (L72 OR L73)

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L78  ANSWER 1 OF 26  ZCAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2008:234466  ZCAPLUS  Full-text
DOCUMENT NUMBER:          148:403101
TITLE:                    Efficient Synthesis of (3R,3aS,6aR)-Hexahydrofuro[2,3-
                          b]furan-3-ol from Glycolaldehyde
AUTHOR(S):                Canoy, Will L.; Cooley, Bob E.; Corona, John A.;
                          Lovelace, Thomas C.; Millar, Alan; Weber, Aimee M.;
                          Xie, Shiping; Zhang, Yong
CORPORATE SOURCE:         Chemical Development, GlaxoSmithKline, Research
                          Triangle Park, NC, 27709, USA
SOURCE:                   Organic Letters (2008), 10(6), 1103-1106
                          CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER:                American Chemical Society
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
OTHER SOURCE(S):          CASREACT 148:403101
GI
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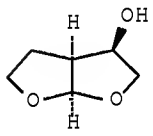

I

AB A one-step diastereoselective (up to 98:2) synthesis of the bis-furan alc. I, the unit which is present in Darunavir and other HIV drug candidates, has been achieved utilizing the novel cyclization of glycolaldehyde and 2,3-dihydrofuran. The cycloaddn. was catalyzed by a variety of catalysts including those formed from tin(II) triflate and common chiral ligands such as BINAP and Evans's BOX ligands. An efficient and unique enzymic process enhanced the enantiomeric purity to provide the target in optically pure form.

```
CC   28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
IT   156928-09-5P
     RL: BPN (Biosynthetic preparation); SPN (Synthetic preparation); BIOL
     (Biological study); PREP (Preparation)
        (efficient asym. synthesis of hexahydrofuro[2,3-b]furanol from
        glycolaldehyde and dihydrofuran)
IT   156928-10-8P 869565-59-3P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (efficient asym. synthesis of hexahydrofuro[2,3-b]furanol from
        glycolaldehyde and dihydrofuran)
IT   156928-09-5P
     RL: BPN (Biosynthetic preparation); SPN (Synthetic preparation); BIOL
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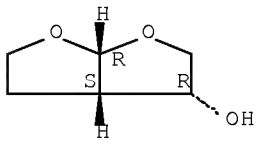
(Biological study); PREP (Preparation)
(efficient asym. synthesis of hexahydrofuro[2,3-b]furanol from glycolaldehyde and dihydrofuran)

RN 156928-09-5 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

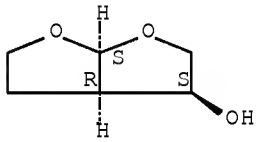
Absolute stereochemistry. Rotation (-).



IT 156928-10-8P 869565-59-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(efficient asym. synthesis of hexahydrofuro[2,3-b]furanol from glycolaldehyde and dihydrofuran)

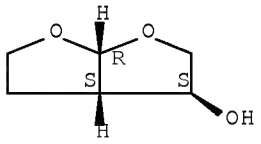
RN 156928-10-8 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3S,3aR,6aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 869565-59-3 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aR,6aS)-rel- (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L78 ANSWER 2 OF 26 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1275513 ZCAPLUS Full-text
DOCUMENT NUMBER: 147:502340
TITLE: Process for preparation of carbamic acid bisfuranyl esters as HIV protease inhibitors and their use in the treatment of retroviral infection
INVENTOR(S): Crawford, Kenneth R.; Dowdy, Eric D.; Gutierrez,

	Arnold; Polniaszek, Richard P.; Yu, Richard Hung Chiu
PATENT ASSIGNEE(S):	Gilead Sciences, Inc., USA
SOURCE:	PCT Int. Appl., 58pp.
	CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

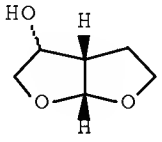
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007126812	A2	20071108	WO 2007-US7564	20070329
WO 2007126812	A3	20071221		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

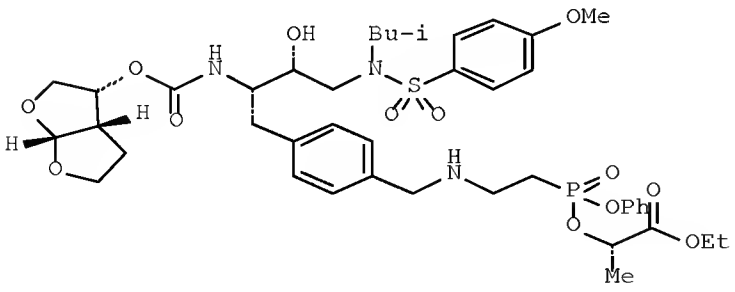
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

US 20080004242	A1	20080103	US 2007-729522	20070329
PRIORITY APPLN. INFO.:			US 2006-787126P	P 20060329
OTHER SOURCE(S):	CASREACT 147:502340			

GI



I

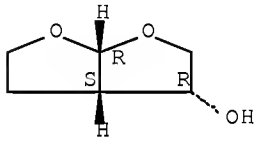


II

AB A process for the synthesis of bisfuran intermediates, e.g., I useful for preparing antiviral HIV protease inhibitor compds. is hereby disclosed. Example compound II was prepared as adipic acid salt and succinic acid salts, using intermediate I as the key component in the preparation The invention compds. were evaluated for their HIV protease inhibitory activity (no data).

CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63
IT 156928-09-5P
RL: BSU (Biological study, unclassified); IMF (Industrial manufacture); PUR (Purification or recovery); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of carbamic acid bisfuranyl ester compds. as HIV protease inhibitors useful in treatment and prevention of retroviral infection)
IT 156928-09-5P
RL: BSU (Biological study, unclassified); IMF (Industrial manufacture); PUR (Purification or recovery); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of carbamic acid bisfuranyl ester compds. as HIV protease inhibitors useful in treatment and prevention of retroviral infection)
RN 156928-09-5 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L78 ANSWER 3 OF 26 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1131417 ZCAPLUS Full-text
DOCUMENT NUMBER: 148:33642
TITLE: Research and Development of an Efficient Synthesis of Hexahydrofuro[2,3-b]furan-3-ol Moiety-A Key Component of the HIV Protease Inhibitor Candidates
AUTHOR(S): Yu, Richard H.; Polniaszek, Richard P.; Becker, Mark W.; Cook, Charles M.; Yu, Lok Him L.
CORPORATE SOURCE: Process Research Department, Gilead Sciences, Inc., Foster City, CA, 94404, USA
SOURCE: Organic Process Research & Development (2007), 11(6), 972-980
CODEN: OPRDFK; ISSN: 1083-6160
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 148:33642
AB A highly efficient method for the synthesis of racemic hexahydrofuro[2,3-b]furan-3-ol has been developed utilizing a lanthanide catalyst, such as Yb(fod)3, to promote condensation of 2,3-dihydrofuran and glycolaldehyde dimer. Access to either optically enriched enantiomer of bisfuran alc. can be obtained by using this method employing chiral ligands with the lanthanide catalyst. This method has been demonstrated to be a robust and scalable process with potential application for the construction of a variety of furo[2,3-b]furan derivs.
CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
IT 156928-09-5P
RL: BPN (Biosynthetic preparation); IMF (Industrial manufacture); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

(scalable synthesis of enantiopure hexahydrofuro[2,3-b]furan-3-ol as a key component of the HIV protease inhibitor candidates)

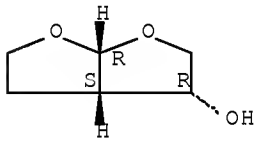
IT 162119-33-7P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(scalable synthesis of enantiopure hexahydrofuro[2,3-b]furan-3-ol as a key component of the HIV protease inhibitor candidates)

IT 156928-10-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(scalable synthesis of enantiopure hexahydrofuro[2,3-b]furan-3-ol as a key component of the HIV protease inhibitor candidates)

IT 156928-09-5P
RL: BPN (Biosynthetic preparation); IMF (Industrial manufacture); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(scalable synthesis of enantiopure hexahydrofuro[2,3-b]furan-3-ol as a key component of the HIV protease inhibitor candidates)

RN 156928-09-5 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

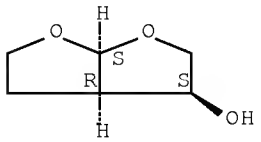
Absolute stereochemistry. Rotation (-).



IT 162119-33-7P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(scalable synthesis of enantiopure hexahydrofuro[2,3-b]furan-3-ol as a key component of the HIV protease inhibitor candidates)

RN 162119-33-7 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)-rel- (CA INDEX NAME)

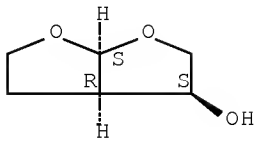
Relative stereochemistry.



IT 156928-10-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(scalable synthesis of enantiopure hexahydrofuro[2,3-b]furan-3-ol as a key component of the HIV protease inhibitor candidates)

RN 156928-10-8 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3S,3aR,6aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



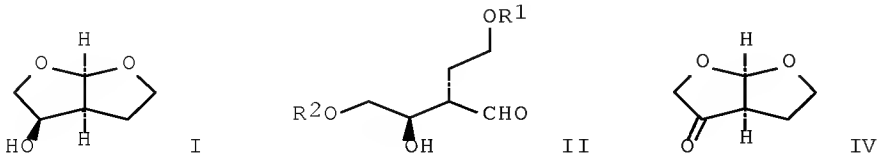
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L78 ANSWER 4 OF 26 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1310631 ZCAPLUS Full-text
DOCUMENT NUMBER: 146:62694
TITLE: Method for producing hexahydrofuro[2,3-b]furan-3-ol derivative
INVENTOR(S): Ikemoto, Tetsuya; Watanabe, Yosuke
PATENT ASSIGNEE(S): Sumitomo Chemical Company, Limited, Japan
SOURCE: PCT Int. Appl., 54pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006132390	A1	20061214	WO 2006-JP311682	20060605
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
JP 2007131613	A	20070531	JP 2006-136950	20060516
EP 1889826	A1	20080220	EP 2006-747271	20060605
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				

PRIORITY APPLN. INFO.: JP 2005-166020 A 20050606
JP 2005-300487 A 20051014
WO 2006-JP311682 W 20060605

OTHER SOURCE(S): MARPAT 146:62694
GI



I II IV

AB There is disclosed a method for producing (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-ol (I) which comprises a step for obtaining a compound (II) by enantioselective addition reaction of an aldehyde of formula R1O(CH2)3CHO (R1 = hydroxy-protecting group) with an acetaldehyde derivative of formula R2OCH2CHO (R2 = hydroxy-protecting) in the presence of an optionally substituted cyclic secondary amine, and a step for obtaining the compound II by removing R1 and R2 from the compound II sequentially or at a time and then cyclizing the compound from which the R1 and R2 are removed. A method for producing a high-purity compound I, an intermediate thereof, and a method for producing the intermediate are also disclosed. Thus, a solution of 120.1 g 2-benzyloxyacetaldehyde in 264 mL DMF was cooled to 4°, treated with 9.20 g L-proline and then dropwise with a solution of 71.3 g 4-benzyloxybutyraldehyde in 128 mL DMF over 12 h, and the resulting mixture was stirred for 31 h to give, after workup, 193.2 g crude (2S,3R)-4-benzyloxy-2-(2-benzyloxyethyl)-3-hydroxybutyraldehyde II (R1 = R2 = benzyl) (III). The crude III (193.2 g) was dissolved in 300 mL ethanol, treated with 8 g 10% Pd-C (50% wet) and 30 mL 5% HCl solution, hydrogenated at 22-30° under H pressure of 5 atmospheric for 19 h, filtered to remove the catalyst, treated with 7.0 g K2CO3, and stirred for 1 h. The solvent was distilled away to give an oil which was treated with 200 mL ethanol and Na2SO4 , stirred, filtered, and concentrated to give 98.3 g crude I in a (3R,3aS,6aR)/(3S,3aS,6aR) diastereomeric ratio of 3.8/1 as a yellow liquid The obtained crude mixture (18.9 g) containing I 7.93, (3S,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-ol 2.07, (3S,3aR,6aS)-hexahydrofuro[2,3-b]furan-3-ol 0.05, and (3R,3aR,6aS)-hexahydrofuro[2,3-b]furan-3-ol 0.05 g was dissolved in 112 mL EtOAc, treated with 27.1 g K2HPO4, 0.5 g KBr, and 61 mg 2,2,6,6-tetramethylpiperidinyl-1-oxy, cooled to 0°, treated dropwise with 123.9 g aqueous NaClO2 (14% effective Cl content) at ≤15°, and stirred for 1 h to give, after workup and recrystn. from 2-propanol, 73% (3aR,6aR)-tetrahydrofuro[2,3-b]furan- 3(2H)-one (IV) (98% purity, 100% ee). IV (5 g) was suspended in 15 mL ethanol, cooled to -15°, treated with 0.43 g NaBH4 in portions, stirred for 2 h, neutralized with 1.2 g 35% aqueous HCl solution to give, after workup, 96.6% I (4.81 g) in a (3R,3aS,6aR)/(3S,3aS,6aR) diastereomeric ratio of 98.2/1.8 as a colorless to light yellow liquid

CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))

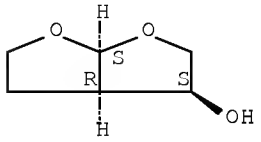
IT 156928-10-8P, (3S,3aR,6aS)-Hexahydrofuro[2,3-b]furan-3-ol
252873-00-0P, (3R,3aR,6aS)-Hexahydrofuro[2,3-b]furan-3-ol
RL: BYP (Byproduct); PREP (Preparation)
(preparation of chiral hexahydrofuro[2,3-b]furan-3-ol by enantioselective addition reaction of hydroxybutyraldehyde derivative and hydroxyacetaldehyde
derivative in presence of L-proline)

IT 4541-14-4P, 4-Benzyloxybutanol 4799-67-1P, 3-Benzyloxy-1,2-propanediol
5470-84-8P, 4-Benzyloxybutyraldehyde 60656-87-3P, 2-Benzyloxyacetaldehyde 156928-09-5P, (3R,3aS,6aR)-Hexahydrofuro[2,3-b]furan-3-ol 252873-50-0P, (3S,3aS,6aR)-Hexahydrofuro[2,3-b]furan-3-ol 809286-93-9P, (3aR,6aR)-Tetrahydrofuro[2,3-b]furan-3(2H)-one 916898-59-4P, (2S,3R)-4-Benzyloxy-2-(2-benzyloxyethyl)-3-hydroxybutyraldehyde
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of chiral hexahydrofuro[2,3-b]furan-3-ol by enantioselective addition reaction of hydroxybutyraldehyde derivative and hydroxyacetaldehyde
derivative in presence of L-proline)

IT 156928-10-8P, (3S,3aR,6aS)-Hexahydrofuro[2,3-b]furan-3-ol
252873-00-0P, (3R,3aR,6aS)-Hexahydrofuro[2,3-b]furan-3-ol
RL: BYP (Byproduct); PREP (Preparation)
(preparation of chiral hexahydrofuro[2,3-b]furan-3-ol by enantioselective addition reaction of hydroxybutyraldehyde derivative and hydroxyacetaldehyde
derivative in presence of L-proline)

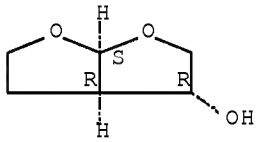
RN 156928-10-8 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3S,3aR,6aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 252873-00-0 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aR,6aS)- (CA INDEX NAME)

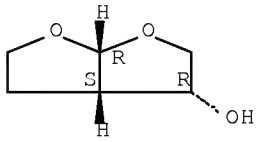
Absolute stereochemistry.



IT 156928-09-5P, (3R,3aS,6aR)-Hexahydrofuro[2,3-b]furan-3-ol
252873-50-0P, (3S,3aS,6aR)-Hexahydrofuro[2,3-b]furan-3-ol
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of chiral hexahydrofuro[2,3-b]furan-3-ol by enantioselective addition reaction of hydroxybutyraldehyde derivative and hydroxyacetaldehyde
derivative in presence of L-proline)

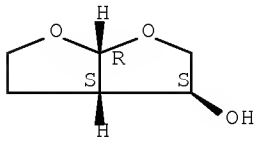
RN 156928-09-5 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 252873-50-0 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3S,3aS,6aR)- (CA INDEX NAME)

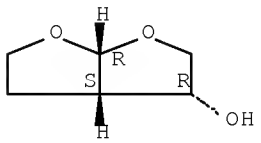
Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L78 ANSWER 5 OF 26 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1143137 ZCAPLUS Full-text
DOCUMENT NUMBER: 146:62621
TITLE: A stereoselective anti-aldol route to (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-ol: a key ligand for a new generation of HIV protease inhibitors
AUTHOR(S): Ghosh, Arun K.; Li, Jianfeng; Perali, Ramu Sridhar
CORPORATE SOURCE: Departments of Chemistry and Medicinal Chemistry, Purdue University, West Lafayette, IN, 47907, USA
SOURCE: Synthesis (2006), (18), 3015-3018
CODEN: SYNTBF; ISSN: 0039-7881
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 146:62621
AB A stereoselective synthesis of (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3- ol, an important high affinity P2-ligand, in high enantiomeric excess (>99%) is reported. The synthesis features an ester-derived titanium enolate based highly stereoselective anti-aldol reaction as the key step.
CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 33
IT 156928-09-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(stereoselective anti-aldol route to (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-ol, a key ligand for a new generation of HIV protease inhibitors)
IT 156928-09-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(stereoselective anti-aldol route to (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-ol, a key ligand for a new generation of HIV protease inhibitors)
RN 156928-09-5 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



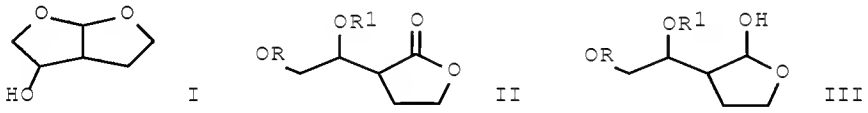
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L78 ANSWER 6 OF 26 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1219971 ZCAPLUS Full-text
DOCUMENT NUMBER: 143:477952
TITLE: Production method of hexahydrofurofuranol derivative, intermediate therefor and production method thereof
INVENTOR(S): Ikemoto, Tetsuya; Piao, Dongguo
PATENT ASSIGNEE(S): Sumitomo Chemical Company, Limited, Japan
SOURCE: U.S. Pat. Appl. Publ., 41 pp., Cont.-in-part of U.S. Ser. No. 744,733.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050256322	A1	20051117	US 2005-64573	20050224
JP 2004107315	A	20040408	JP 2002-382584	20021227
JP 2005008530	A	20050113	JP 2003-171303	20030616
US 20040162340	A1	20040819	US 2003-744733	20031223
US 6867321	B2	20050315		

PRIORITY APPLN. INFO.:
JP 2002-382584 A 20021227
JP 2003-171303 A 20030616
US 2003-744733 A2 20031223
JP 2002-212680 A 20020722

OTHER SOURCE(S): CASREACT 143:477952; MARPAT 143:477952
GI



AB A process for the preparation of hexahydrofurofuranols of formula I and their intermediates of formula II [R, R1 = H, hydroxyl protecting group, etc.] is disclosed. Thus, to a solution of compound (2R,4'R)-II [R,R1 = C(Me)2] prepared from 2-benzyloxyacetyl-γ-butyrolactone in 2 steps, in THF was added DIBAL at -70 degrees to provide (3R,4'R)-III [R,R1 = C(Me)2]. A mixture of (3R,4'R)-III [R,R1 = C(Me)2] and 6N HCl in THF was stirred overnight at room temperature Treatment with K2CO3 afforded compound (3R,3aR,6aS)-I in 88% ee. Mitsunobu inversion of (3R,3aR,6aS)-I at the C3 position followed by hydrolysis provided (3S,3aR,6aS)-I in 88% ee. Compds. I are useful intermediates for the preparation of anti-AIDS agents. The disclosed process provides an effective preparation method for hexahydrofurofuranols without using hazardous materials, e.g. oxone, etc.

IC ICM C07D493-02
INCL 549464000
CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
IT 54555-84-9P 58841-52-4P 81366-59-8P 109789-18-6P

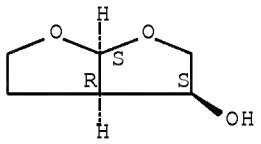
162119-33-7P 177987-29-0P 252873-00-0P
252873-50-0P 676998-88-2P 676998-89-3P 676998-90-6P
676998-91-7P 676998-92-8P 676998-93-9P 676998-94-0P 676998-97-3P
676998-98-4P 676998-99-5P 676999-00-1P 676999-02-3P 725264-56-2P
725264-57-3P 725264-58-4P 725264-59-5P 725264-60-8P 725264-61-9P
725264-62-0P 725264-63-1P 725264-64-2P 725264-65-3P 725264-66-4P
725264-67-5P 725264-69-7P 869565-57-1P 869565-58-2P
869565-59-3P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for the preparation of hexahydrofurofuranol derivs.)

IT 156928-09-5P 156928-10-8P 676999-06-7P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for the preparation of hexahydrofurofuranol derivs.)

IT 162119-33-7P 252873-00-0P 252873-50-0P
869565-59-3P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for the preparation of hexahydrofurofuranol derivs.)

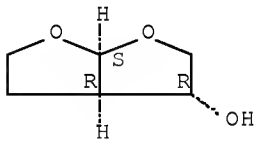
RN 162119-33-7 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)-rel- (CA INDEX NAME)

Relative stereochemistry.



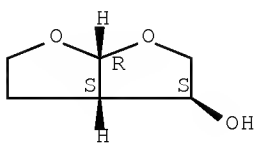
RN 252873-00-0 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aR,6aS)- (CA INDEX NAME)

Absolute stereochemistry.



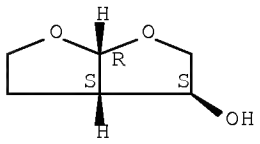
RN 252873-50-0 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3S,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



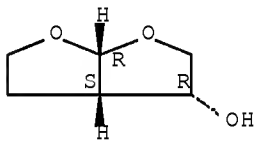
RN 869565-59-3 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aR,6aS)-rel- (CA INDEX NAME)

Relative stereochemistry.



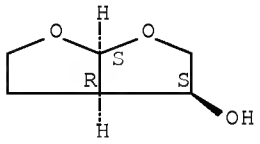
IT 156928-09-5P 156928-10-8P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for the preparation of hexahydrofurofuranol derivs.)
RN 156928-09-5 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 156928-10-8 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3S,3aR,6aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L78 ANSWER 7 OF 26 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:14172 ZCAPLUS Full-text
DOCUMENT NUMBER: 142:114047
TITLE: A preparation of furofuranyl derivative, useful as inhibitor of HIV aspartyl protease
INVENTOR(S): Roberts, John Charles; Toczko, Jennifer Fell
PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA; Martin, Michael Tolar
SOURCE: PCT Int. Appl., 36 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

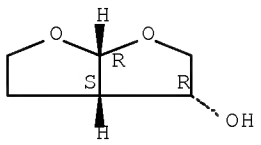
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005000249	A2	20050106	WO 2004-US20353	20040625
WO 2005000249	A3	20050407		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1638960	A2	20060329	EP 2004-777060	20040625
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR				
JP 2007521277	T	20070802	JP 2006-517643	20040625
US 20060148865	A1	20060706	US 2005-560500	20051212
PRIORITY APPLN. INFO.:			US 2003-483002P P	20030627
			WO 2004-US20353 W	20040625

OTHER SOURCE(S): CASREACT 142:114047
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a preparation of furofuranyl derivative I, useful as inhibitor of HIV aspartyl protease (no biol. data). For instance, I was prepared via deprotection of II and coupling with III with a yield of 90% (example 2).
IC ICM A61K
CC 28-7 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 45
IT 96406-00-7P 156928-09-5P 192725-55-6P 313680-94-3P
640289-31-2P 820250-06-4P 820250-07-5P 820250-08-6P 820250-09-7P
820250-10-0P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of furofuranyl derivative useful as inhibitor of HIV aspartyl protease)
IT 156928-09-5P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of furofuranyl derivative useful as inhibitor of HIV aspartyl protease)
RN 156928-09-5 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L78 ANSWER 8 OF 26 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:870349 ZCAPLUS Full-text
DOCUMENT NUMBER: 142:56210
TITLE: Stereoselective Photochemical 1,3-Dioxolane Addition to 5-Alkoxymethyl-2(5H)-furanone: Synthesis of Bis-tetrahydrofuranyl Ligand for HIV Protease Inhibitor UIC-94017 (TMC-114)
AUTHOR(S): Ghosh, Arun K.; Leshchenko, Sofiya; Noetzel, Marcus
CORPORATE SOURCE: Department of Chemistry, University of Illinois at Chicago, Chicago, IL, 60607, USA
SOURCE: Journal of Organic Chemistry (2004), 69(23), 7822-7829
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:56210
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB HIV protease inhibitor UIC-94017 I is prepared using the stereoselective photochem. addition of 1,3-dioxolane to nonracemic 5-substituted 2-furanones to yield dioxolanylfuranones as the key step. Nonracemic 5-(benzyloxymethyl)-2-furanone II (R = PhCH2) is prepared in 4-7 steps from benzyloxyacetaldehyde using a lipase-mediated resolution to generate the desired absolute stereochem. Addition of vinylmagnesium bromide to benzyloxyacetaldehyde yields 1-(benzyloxy)-3-buten-2-ol which undergoes enantioselective acylation with isopropenyl acetate in the presence of lipase PS-30 to yield (S)-1-(benzyloxy)-3-buten-2-ol in 49% yield and 99% ee and (R)-1-(benzyloxy)-3-buten-2-ol acetate in 49% yield (which can be converted to the desired alc. in 3 steps and 82% yield and 81% ee). Acylation of (S)-1-(benzyloxy)-3-buten-2-ol with acryloyl chloride followed by ring closure with the 2nd generation Grubbs ruthenium metathesis catalyst provides II (R = PhCH2). II [R = Me3CSi(Me)2, Ac, Me3CCO, PhCO, 2-tetrahydropyranyl] are also prepared by a three-step procedure from isopropylidene-D-glycerol. Irradiation of II [R = PhCH2, Me3CSi(Me)2, Ac, Me3CCO, PhCO, 2-tetrahydropyranyl] and 1,3-dioxolane in the presence of benzophenone yields dioxolanylfuranones III [R = PhCH2, Me3CSi(Me)2, Ac, Me3CCO, PhCO, 2-tetrahydropyranyl] in 36-93% yields and with 76:24-97:3 selectivity for the trans stereoisomers (in all but one case ≥96:4 stereoselectivity). Reductive cleavage of the benzyl group of III (R = PhCH2), lithium aluminum hydride reduction of the lactone and acid-mediated cyclization yields the alc. epimer of desired hexahydrofurofuranol IV; either oxidation of the alc. to the ketone followed by reduction or Mitsunobu inversion followed by hydrolysis of the p-nitrobenzoate ester yields IV stereoselectively. Ring opening of (S,S)-N-Boc-α-benzyloxiranemethanamine with isobutylamine followed by sulfonylation of the secondary amine with p-

nitrobenzenesulfonyl chloride yields intermediate carbamate V. Reduction of the nitro group of V, removal of the Boc group, and coupling with the N-hydroxysuccinimidyl carbonate mixed ester of IV yields I.

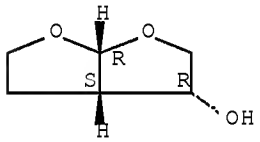
CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))

IT 156928-09-5P 206361-99-1P, UIC-94017 252873-50-0P
253265-97-3P 681463-03-6P 809286-93-9P
RL: BPN (Biosynthetic preparation); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(stereoselective preparation of a nonracemic dioxolanylfuranone by photochem. addition of 1,3-dioxolane to nonracemic 5-(benzyloxymethyl)-2-furanone and its use in the preparation of the HIV protease inhibitor UIC-94017)

IT 156928-09-5P 252873-50-0P
RL: BPN (Biosynthetic preparation); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(stereoselective preparation of a nonracemic dioxolanylfuranone by photochem. addition of 1,3-dioxolane to nonracemic 5-(benzyloxymethyl)-2-furanone and its use in the preparation of the HIV protease inhibitor UIC-94017)

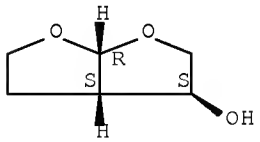
RN 156928-09-5 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 252873-50-0 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3S,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L78 ANSWER 9 OF 26 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:807698 ZCAPLUS Full-text
DOCUMENT NUMBER: 142:211389
TITLE: Discovery and Selection of TMC114, a Next Generation HIV-1 Protease Inhibitor
AUTHOR(S): Surleraux, Dominique L. N. G.; Tahri, Abdellah; Verschueren, Wim G.; Pille, Geert M. E.; de Kock,

Herman A.; Jonckers, Tim H. M.; Peeters, Anik; De Meyer, Sandra; Azijn, Hilde; Pauwels, Rudi; de Bethune, Marie-Pierre; King, Nancy M.; Prabu-Jeyabalan, Moses; Schiffer, Celia A.; Wigerinck, Piet B. T. P.
CORPORATE SOURCE: Tibotec BVBA, Mechelen, B-2800, Belg.
SOURCE: Journal of Medicinal Chemistry (2005), 48(6), 1813-1822
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:211389

AB The screening of known HIV-1 protease inhibitors against a panel of multidrug-resistant viruses revealed the potent activity of TMC126 on drug-resistant mutants. In comparison to amprenavir, the improved affinity of TMC126 is largely the result of one extra hydrogen bond to the backbone of the protein in the P2 pocket. Modification of the substitution pattern on the phenylsulfonamide P2' substituent of TMC126 created an interesting SAR, with the close analog TMC114 being found to have a similar antiviral activity against the mutant and the wild-type viruses. X-ray and thermodn. studies on both wild-type and mutant enzymes showed an extremely high enthalpy driven affinity of TMC114 for HIV-1 protease. In vitro selection of mutants resistant to TMC114 starting from wild-type virus proved to be extremely difficult; this was not the case for other close analogs. Therefore, the extra H-bond to the backbone in the P2 pocket cannot be the only explanation for the interesting antiviral profile of TMC114. Absorption studies in animals indicated that TMC114 has pharmacokinetic properties comparable to currently approved HIV-1 protease inhibitors.

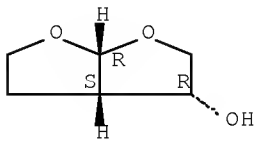
CC 1-3 (Pharmacology)

IT 156928-09-5P 156928-10-8P 157566-91-1P 157567-13-0P
159005-71-7P 160230-53-5P 160232-08-6P 162020-29-3P 169280-56-2P
169280-63-1P 169280-71-1P 174303-68-5P 191226-98-9P 206362-03-0P
244641-42-7P 251105-80-3P 252873-00-0P 252873-50-0P
253265-97-3P 253265-98-4P 553644-88-5P 553645-08-2P 553645-09-3P
695815-04-4P 799241-79-5P 799241-80-8P 799241-81-9P 799241-82-0P
799241-83-1P 799241-85-3P 799241-86-4P 799241-87-5P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(discovery and selection of TMC114, a next generation HIV-1 protease inhibitor)

IT 156928-09-5P 156928-10-8P 252873-00-0P
252873-50-0P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(discovery and selection of TMC114, a next generation HIV-1 protease inhibitor)

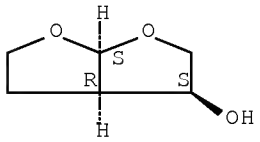
RN 156928-09-5 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



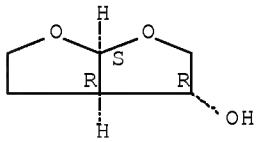
RN 156928-10-8 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3S,3aR,6aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



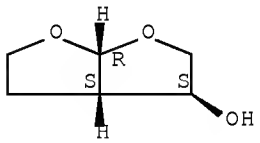
RN 252873-00-0 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aR,6aS)- (CA INDEX NAME)

Absolute stereochemistry.



RN 252873-50-0 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3S,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



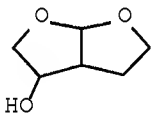
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L78 ANSWER 10 OF 26 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:589551 ZCAPLUS Full-text
DOCUMENT NUMBER: 141:140415
TITLE: Hexahydrofurofuranol derivatives and their intermediates and process for preparation thereof
INVENTOR(S): Ikemoto, Tetsuya; Piao, Dongguo
PATENT ASSIGNEE(S): Sumika Fine Chemicals Co., Ltd., Japan
SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

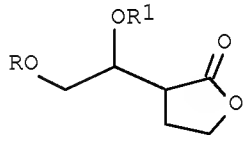
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004060895	A1	20040722	WO 2003-JP13685	20031027
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
JP 2004107315	A	20040408	JP 2002-382584	20021227
JP 2005008530	A	20050113	JP 2003-171303	20030616
AU 2003275675	A1	20040729	AU 2003-275675	20031027
EP 1589018	A1	20051026	EP 2003-758920	20031027
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
IN 2005CN01699	A	20070622	IN 2005-CN1699	20050726
PRIORITY APPLN. INFO.:			JP 2002-382584 A	20021227
			JP 2003-171303 A	20030616
			JP 2002-212680 A	20020722
			WO 2003-JP13685 W	20031027

OTHER SOURCE(S): MARPAT 141:140415

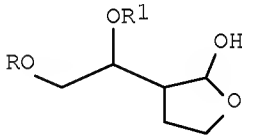
GI



I



II



III

AB Process for the preparation of hexahydrofurofuranols I and their intermediates II [R, R1 = H, protecting group of OH, etc.] were disclosed. Title compds., e.g., II are claimed. For example, to a solution of compound (2R,4'R)-II [RR1 = C(CH3)2], e.g., prepared from 2-benzyloxyacetyl-γ- butyrolactone in 2 steps, (17.7 g)in THF (150 mL) was added 1.0 M DIBAL (100 mL) at −70 °C. After stirring for 3.5 h and aqueous work-up, (3R,4'R)-III [RR1 = C(CH3)2] (13.8 g) was obtained. A mixture of (3R,4'R)-III [RR1 = C(CH3)2] (13.8 g), 6 N HCl (4 mL) in THF (120 mL) was stirred at room temperature overnight. Then, treatment with K2CO3 (25 g) furnished compound (3R,3aR,6aS)-I (2.8 g) in 88%

ee. Epimerization of (3R,3aR,6aS)-I at C3 position using benzoic acid under Mitsunobu condition followed by hydrolysis afforded (3S,3aR,6aS)-I in 78% yield, 88% ee. Of note, compds. I are useful intermediates for the preparation of anti-AIDS agents. The disclosed process provided effective preparation method for Hexahydrofurofuranols without using hazardous materials, e.g., oxone, etc.

IC ICM C07D493-04
ICS C07D407-04; C07D307-32

CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))

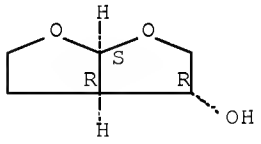
IT 54555-84-9P, 2-Benzyloxyethyl iodide 58841-52-4P, 2-Benzyloxyethylmethanesulfonate 81366-59-8P 177987-29-0P 252873-00-0P 252873-50-0P 676998-88-2P 676998-89-3P 676998-90-6P 676998-91-7P 676998-92-8P 676998-93-9P 676998-94-0P 676998-97-3P 676998-98-4P 676998-99-5P 676999-00-1P 676999-02-3P 676999-06-7P 725264-56-2P 725264-57-3P 725264-58-4P 725264-59-5P 725264-60-8P 725264-61-9P 725264-62-0P 725264-63-1P 725264-64-2P 725264-65-3P 725264-66-4P 725264-67-5P 725264-69-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for preparation of hexahydrofurofuranol derivs. via reduction of lactone followed by one-pot reaction of deacetalization and cyclization)

IT 156928-09-5P, 3R,3AS,6aR-hexahydrofuro[2,3-b]furan-3-ol 156928-10-8P 162119-33-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(process for preparation of hexahydrofurofuranol derivs. via reduction of lactone followed by one-pot reaction of deacetalization and cyclization)

IT 252873-00-0P 252873-50-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for preparation of hexahydrofurofuranol derivs. via reduction of lactone followed by one-pot reaction of deacetalization and cyclization)

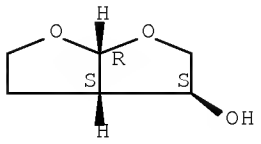
RN 252873-00-0 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aR,6aS)- (CA INDEX NAME)

Absolute stereochemistry.



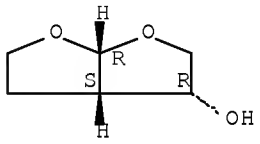
RN 252873-50-0 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3S,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



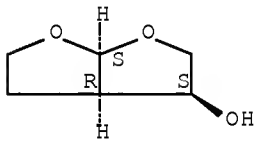
IT 156928-09-5P, 3R,3AS,6aR-hexahydrofuro[2,3-b]furan-3-ol
156928-10-8P 162119-33-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(process for preparation of hexahydrofurofuranol derivs. via reduction of lactone followed by one-pot reaction of deacetalization and cyclization)
RN 156928-09-5 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



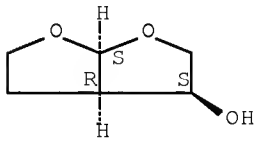
RN 156928-10-8 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3S,3aR,6aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 162119-33-7 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)-rel- (CA INDEX NAME)

Relative stereochemistry.



L78 ANSWER 11 OF 26 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:333721 ZCAPLUS Full-text
DOCUMENT NUMBER: 140:357319
TITLE: Method of preparing (3R,3aS,6aR)-3-hydroxyhexahydrofuro[2,3-b]furan and related compounds
INVENTOR(S): Ghosh, Arun K.; Leshchenko, Sofiya; Noetzel, Marcus W.
PATENT ASSIGNEE(S): The Board of Trustees of the University of Illinois,

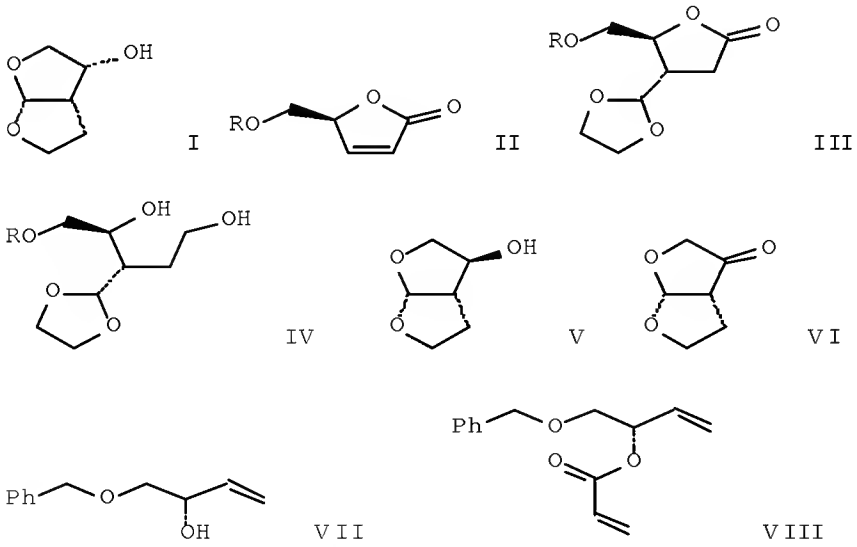
	USA
SOURCE:	PCT Int. Appl., 63 pp.
	CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004033462	A2	20040422	WO 2003-US32029	20031008
WO 2004033462	A3	20040930		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003287038	A1	20040504	AU 2003-287038	20031008
US 20040127727	A1	20040701	US 2003-681637	20031008
US 6919465	B2	20050719		

PRIORITY APPLN. INFO.:	US 2002-417379P	P	20021009
	WO 2003-US32029	W	20031008
OTHER SOURCE(S):	CASREACT 140:357319; MARPAT 140:357319		

GI



AB A method of synthesizing (3R,3aS,6aR)-3-hydroxyhexahydrofuro[2,3-b]furan (I), and related compds., in high yield and high enantiomeric selectivity is disclosed. The above process comprises (a) optionally reacting (5S)-

hydroxymethyl-5H-furan-2-one (II; R = H) with a compound capable of positioning a protecting group at the hydroxy position to provide a protected furan-2-one II (R = protecting group); (b) subjecting II (R = H) or protected II (R = protecting group) of optional step (a) to a photochem. addition reaction in the presence of 1,3-dioxolane to provide a 1,3-dioxolan-substituted furan-2-one (III; R = H, protecting group); (c) reducing the compound III to a reduced product (IV; R = H, protecting group), then hydrolyzing the reduced product to provide a product (V) (d) oxidizing the product V to provide a product (VI) and (e) reducing the product VI to provide I. The compound I is an intermediate for several highly potent HIV inhibitors. Also disclosed is a method of manufacturing the compound II which comprising the steps of (a) subjecting (±)-1-(benzyloxy)but-3-en-2-ol to an enzymic acylation using immobilized lipase PS-30 and isopropenyl acetate to provide (S)-1-(benzyloxy)but-3-en-2-ol (VII); (b) reacting the product VII with acryloyl chloride to provide (S)-1-(benzyloxy)but-3-en-2-yl acrylate (VIII); and (c) interacting the product VIII with Grubbs catalyst [Cl2(PCy3)(IMes)Ru:CHC6H5] (metathesis cyclization) to provide II.

IC ICM C07D493-04

CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))

IT 72605-53-9P 81661-46-3P 85846-83-9P 93553-66-3P, 1-(Benzyloxy)but-3-en-2-ol 96086-02-1P 105122-15-4P 113426-94-1P 128387-70-2P 139230-94-7P 140156-47-4P 252873-50-0P 681462-91-9P, (5S)-5-[(Trimethylsilyloxy)methyl]-5H-furan-2-one 681462-92-0P 681462-93-1P 681462-94-2P 681462-95-3P, (4S,5S)-4-([1,3]Dioxolan-2-yl)-5-[(tetrahydropyran-2-yloxy)methyl]tetrahydrofuran-2-one 681462-97-5P 681462-99-7P 681463-01-4P 681463-02-5P 681463-03-6P 681463-04-7P, (2S,3S)-3-[1,3]Dioxolan-2-ylpentane-1,2,5-triol 681463-06-9P, (4S,5S)-5-[(Trimethylsilyloxy)methyl]-4-([1,3]dioxolan-2-yl)tetrahydrofuran-2-one 681463-07-0P 681463-08-1P, (5S)-5-[(Methoxymethoxy)methyl]-5H-furan-2-one
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(stereoselective preparation of (3R,3aS,6aR)-3-hydroxyhexahydrofuro[2,3-b]furan and related compds. with high enantiomeric selectivity)

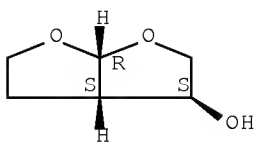
IT 156928-09-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(stereoselective preparation of (3R,3aS,6aR)-3-hydroxyhexahydrofuro[2,3-b]furan and related compds. with high enantiomeric selectivity)

IT 252873-50-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(stereoselective preparation of (3R,3aS,6aR)-3-hydroxyhexahydrofuro[2,3-b]furan and related compds. with high enantiomeric selectivity)

RN 252873-50-0 ZCAPLUS

CN Furo[2,3-b]furan-3-ol, hexahydro-, (3S,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



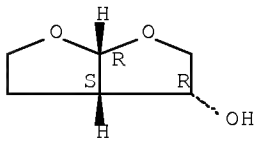
IT 156928-09-5P

RL: SPN (Synthetic preparation); PREP (Preparation)
(stereoselective preparation of (3R,3aS,6aR)-3-hydroxyhexahydrofuro[2,3-b]furan and related compds. with high enantiomeric selectivity)

RN 156928-09-5 ZCAPLUS

CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L78 ANSWER 12 OF 26 ZCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:291182 ZCAPLUS Full-text

DOCUMENT NUMBER: 140:303655

TITLE: Preparation of hexahydrofurofuranol as intermediates for anti-HIV agents via hydroxyethylbutanolides without using toxic agents

INVENTOR(S): Ikemoto, Tetsuya; Park, Dong-guo

PATENT ASSIGNEE(S): Sumika Fine Chemicals Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 54 pp.
CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2004107315	A	20040408	JP 2002-382584	20021227
WO 2004060895	A1	20040722	WO 2003-JP13685	20031027
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003275675	A1	20040729	AU 2003-275675	20031027
EP 1589018	A1	20051026	EP 2003-758920	20031027
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1753898	A	20060329	CN 2003-80109926	20031027
US 20040162340	A1	20040819	US 2003-744733	20031223
US 6867321	B2	20050315		
US 20050256322	A1	20051117	US 2005-64573	20050224
IN 2005CN01699	A	20070622	IN 2005-CN1699	20050726
IN 2007CN02449	A	20070907	IN 2007-CN2449	20070607
PRIORITY APPLN. INFO.:			JP 2002-212680 A	20020722
			JP 2002-382584 A	20021227
			JP 2003-171303 A	20030616

WO 2003-JP13685 W 20031027
US 2003-744733 A2 20031223
IN 2005-CN1699 A3 20050726

OTHER SOURCE(S): MARPAT 140:303655

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Hexahydrofurofuranol was prepared (1) by protection of OH group of hydroxyethylbutanolides I (PG = OH-protecting group; PG' = H), reduction of OH-protected hydroxyethylbutanolides II (R1, R2 = H, lower alkyl, lower alkoxyl, Ph), deprotection of furanols III (R1, R2 = same as above), and cyclization or (2) by protection of OH group of I (PG = OH-protecting group; PG' = H), reduction of I (PG, PG' = OH-protecting group), deprotection of furanols IV (PG, PG' = OH-protecting group), and cyclization. The compds. I (PG = OH-protecting group; PG = H) are prepared by hydroxyethylation of PGOCH2CH(OH)CH2COR'' (PG = OH-protecting group; R'' = lower alkoxy, lower alkylthio) and cyclization via PGOCH2CH(OH)C(COR'')CH2CH2OR''' (PG = OH-protecting group; R'' = lower alkoxy, lower alkylthio; R''' = OH-protecting group, H) and PGOCH2CH(OH)C(CO2H)CH2CH2OR''' (PG, R''' = same as above). Et 4-tert-butoxyacetoacetate was hydrogenated with NaBH4 in MeOH at 5-15° for 1 h, alkylated with 2-(1-ethoxyethoxy)ethyl iodide in the presence of lithium diisopropylamide in THF at room temperature overnight, cyclized with 2-(1-ethoxyethoxy)ethyl iodide in EtOH at room temperature for 6 h, deprotected with F3CCO2H under ice-cooling for 90 min, cyclized with 2,2-dimethoxypropane at room temperature for 2 h, and hydrogenated with diisobutylaluminum hydride in CH2Cl2 at -78° for 1 h to give (3S*,4'R*)-3-[2',2'-dimethyl-(1',3')-dioxolan-4'-yl]tetrahydrofuran-2-ol, which (120 mg) was treated with HCl at room temperature for 20 min to give 50 mg (3R*,3aS*,6aR*)-hexahydrofuro[2,3,b]furan-3-ol.

IC ICM C07D493-04
ICS C07D407-04

CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

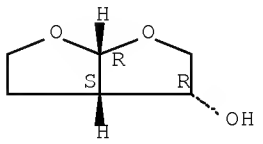
IT 156928-09-5P, (3R*,3AS*,6aR*)-hexahydrofuro[2,3-b]furan-3-ol
156928-10-8P 676999-06-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of hexahydrofurofuranol as anti-HIV agents from hydroxybutanoates via hydroxyethylbutanolides)

IT 156928-09-5P, (3R*,3AS*,6aR*)-hexahydrofuro[2,3-b]furan-3-ol
156928-10-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of hexahydrofurofuranol as anti-HIV agents from hydroxybutanoates via hydroxyethylbutanolides)

RN 156928-09-5 ZCAPLUS

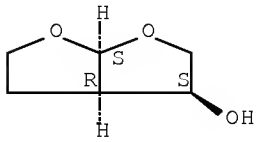
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 156928-10-8 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3S,3aR,6aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L78 ANSWER 13 OF 26 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:20676 ZCAPLUS Full-text
DOCUMENT NUMBER: 140:77015
TITLE: Preparation of stereoisomers of 3α,3aβ,6aβ-hexahydrofuro[2,3-b]furan-3-ol
INVENTOR(S): Doan, Brian Daniel; Patterson, Daniel Edward; Roberts, John C.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004002975	A1	20040108	WO 2003-US20094	20030625
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003247651	A1	20040119	AU 2003-247651	20030625
EP 1532127	A1	20050525	EP 2003-762054	20030625
EP 1532127	B1	20060927		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005533821	T	20051110	JP 2004-517842	20030625
AT 340788	T	20061015	AT 2003-762054	20030625
ES 2268427	T3	20070316	ES 2003-762054	20030625
US 20050261507	A1	20051124	US 2004-517966	20041214
PRIORITY APPLN. INFO.:			US 2002-392677P P	20020627
			WO 2003-US20094 W	20030625

AB A process for the preparation of stereoisomers of 3α,3aβ,6aβ-hexahydrofuro[2,3-b]furan-3-ol is disclosed. For instance, treatment of 2,3-

dihydrofuran with Et chlorooxoacetate (MTBE, Et3N) provides Et α-oxo-4,5-dihydrofuran-3-ylacetate as an oil which is reduced to the diol (THF, LAH) and cyclized (THF/H2O, NBS) to give 3a- bromohexahydrofuro[2,3-b]furan-3-ol as a mixture of 2 diastereomers (3:1). This is reduced (THF, Et3N, H2-Pd/C) and acetylated to give acetic acid hexahydrofuro[2,3-b]furan-3-yl ester. Minor isomer acetates are reacted with a lipase (0.1N Na2HPO4, pH 7.0, 35°, PS-800) and the unreacted acetate starting material (organic extract) is deacylated (MeOH, K2CO3) to give 3R,3aS,6aR-hexahydrofuro[2,3-b]furan-3-ol. Preparation of 3a-bromo analogs are also described. Compds. disclosed herein are useful in the preparation of compds. that may be inhibitors of HIV aspartyl protease. The current process uses inexpensive, nonchiral starting materials and does not rely on heavy metals or photochem. compared to prior art methods.

IC ICM C07D307-26
ICS C07D493-04

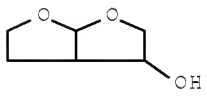
CC 27-6 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63

IT 96406-00-7P 109789-19-7P, Hexahydrofuro[2,3-b]furan-3-ol
162119-35-9P 186488-43-7P 640289-32-3P, 1-(4,5-Dihydrofuran-3-yl)ethane-1,2-diol 640289-33-4P, 3a-Bromohexahydrofuro[2,3-b]furan-3-ol
640289-34-5P, Acetic acid hexahydrofuro[2,3-b]furan-3-yl ester
640289-35-6P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of stereoisomers of 3α,3aβ,6aβ-hexahydrofuro[2,3-b]furan-3-ol via 2,3-dihydrofuran annulation and enzymic resolution)

IT 156928-09-5P, 3R,3AS,6aR-hexahydrofuro[2,3-b]furan-3-ol
640289-30-1P, (3S,3AR,6aR)-3a-bromohexahydrofuro[2,3-b]furan-3-ol
640289-31-2P, rel-(3S,3AR,6aR)-3a-bromohexahydrofuro[2,3-b]furan-3-ol
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of stereoisomers of 3α,3aβ,6aβ-hexahydrofuro[2,3-b]furan-3-ol via 2,3-dihydrofuran annulation and enzymic resolution)

IT 109789-19-7P, Hexahydrofuro[2,3-b]furan-3-ol
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of stereoisomers of 3α,3aβ,6aβ-hexahydrofuro[2,3-b]furan-3-ol via 2,3-dihydrofuran annulation and enzymic resolution)

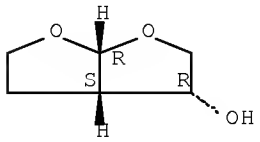
RN 109789-19-7 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro- (CA INDEX NAME)



IT 156928-09-5P, 3R,3AS,6aR-hexahydrofuro[2,3-b]furan-3-ol
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of stereoisomers of 3α,3aβ,6aβ-hexahydrofuro[2,3-b]furan-3-ol via 2,3-dihydrofuran annulation and enzymic resolution)

RN 156928-09-5 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



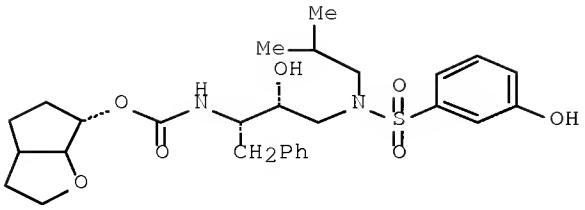
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L78 ANSWER 14 OF 26 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:757713 ZCAPLUS Full-text
DOCUMENT NUMBER: 139:276880
TITLE: Preparation of carbamates as HIV protease inhibitors
INVENTOR(S): Ghosh, Arun K.; Bilcer, Geoffrey M.; Devasamudram, Thippeswamy
PATENT ASSIGNEE(S): The Board of Trustees of the University of Illinois, USA
SOURCE: PCT Int. Appl., 224 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003078438	A1	20030925	WO 2003-US7032		20030307
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 20040039016	A1	20040226	US 2003-382435		20030306
US 7157489	B2	20070102			
CA 2478731	A1	20030925	CA 2003-2478731		20030307
AU 2003213776	A1	20030929	AU 2003-213776		20030307
EP 1485387	A1	20041215	EP 2003-711467		20030307
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
JP 2006504621	T	20060209	JP 2003-576443		20030307
MX 2004PA08858	A	20050620	MX 2004-PA8858		20040910
US 20070082883	A1	20070412	US 2006-593665		20061107

PRIORITY APPLN. INFO.:	US 2002-363628P	P	20020312
	US 2002-433627P	P	20021213
	US 2003-382435	A3	20030306
	WO 2003-US7032	W	20030307

OTHER SOURCE(S): MARPAT 139:276880
GI



I

AB R1O2CNHCH(CH2Ph)CH(OH)CHR4NR2R3 [R1 = alkyl, aryl, heterocyclic; R2 = H, (un)substituted alkyl, NH2, heterocyclic, cycloalkyl; R3 = (un)substituted cyclohexadienylsulfonyl, arylsulfonyl, aroyl, aralkylsulfonyl, heterocyclylsulfonyl, aralkanoyl, heterocyclic, aroylamino, arylsulfonylamino; NR2R3 = heterocyclic; R4 = H, (un)substituted heterocyclylalkyl] were prepared for use as HIV protease inhibitors in treating wild-type HIV and of multidrug-resistant strains of HIV. Thus, the carbamate I was prepared in a multi-step synthesis and has Ki 2.1 nM for inhibition of HIV protease.

IC ICM C07D493-04
ICS C07D491-10; C07D493-10; C07D405-12; C07D405-14; C07D413-14; C07D307-935; C07D409-14; A61K031-34; A61K031-35; A61P031-18; C07D307-00; C07D311-00; C07D209-00

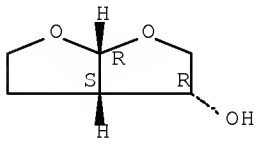
CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

IT 473-84-7P, 2-Hydroxycyclopentanone 603-80-5P, 3-Hydroxy-2-methylbenzoic acid 636-73-7P, 3-Pyridinesulfonic acid 3888-84-4P 4128-00-1P, (S)-3-Amino-2-pyrrolidinone 6281-32-9P, 4-Quinolinemethanol 6668-56-0P, 4-Fluoro-3-nitrobenzenesulfonyl chloride 7134-09-0P 14278-60-5P 26000-56-6P 42417-13-0P 45347-82-8P, 3-Azetidinol 56157-93-8P 62009-36-3P 63640-56-2P 65001-21-0P, 5-Bromo-3-pyridinesulfonyl chloride 69232-47-9P 76282-44-5P 82430-14-6P 101385-90-4P 101469-92-5P 109431-87-0P 111769-26-7P, (R)-3-Aminotetrahydrofuran 120520-91-4P 133034-01-2P 138499-08-8P 141699-55-0P, 1-tert.-Butoxycarbonyl-3-azetidinol 147081-44-5P, (S)-3-Amino-1-tert.-butoxycarbonylpyrrolidine 147081-49-0P, (R)-3-Amino-1-tert.-butoxycarbonylpyrrolidine 156928-09-5P 159006-20-9P 183612-98-8P 193269-78-2P 253265-97-3P 253265-98-4P 329309-68-4P 605653-02-9P 605653-03-0P 605653-04-1P 605653-05-2P 605653-06-3P 605653-10-9P 605653-11-0P 605653-12-1P 605653-13-2P 605653-14-3P 605653-15-4P 605653-16-5P 605653-17-6P 605653-18-7P 605653-19-8P 605653-20-1P 605653-21-2P 605653-22-3P 605653-23-4P 605653-24-5P 605653-28-9P 605653-30-3P 605653-33-6P 605653-35-8P 605653-40-5P 605653-41-6P 605653-52-9P 605654-26-0P 605654-27-1P 605654-97-5P 605654-98-6P 605654-99-7P 605655-00-3P 605655-01-4P 605655-02-5P 605655-03-6P, 1-Oxaspiro[4.4]nonan-6-ol 605655-04-7P 605655-06-9P 605655-07-0P 605655-08-1P 605655-09-2P 605655-10-5P 605655-11-6P 605655-12-7P 605655-13-8P 605655-14-9P 605655-15-0P 605655-16-1P 605655-17-2P 605655-18-3P 605655-19-4P 605655-31-0P 605655-32-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of carbamates as HIV protease inhibitors)

IT 156928-09-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of carbamates as HIV protease inhibitors)

RN 156928-09-5 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L78 ANSWER 15 OF 26 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:242341 ZCAPLUS Full-text
DOCUMENT NUMBER: 138:271663
TITLE: Process for preparing intermediates for HIV aspartyl protease inhibitors, particularly (3α,3aβ,6aβ)-hexahydrofuro[2,3-b]furan-3-ol and its (3R,3aS,6aR)-enantiomer
INVENTOR(S): Doan, Brian Daniel; Davis, Roman D.; Lovelace, Thomas Claiborne
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

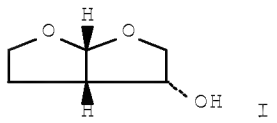
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003024974	A2	20030327	WO 2002-US29315	20020916
WO 2003024974	A3	20040729		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002326925	A1	20030401	AU 2002-326925	20020916
EP 1465897	A2	20041013	EP 2002-761678	20020916
EP 1465897	B1	20060809		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005510467	T	20050421	JP 2003-528821	20020916
AT 335745	T	20060915	AT 2002-761678	20020916
ES 2265052	T3	20070201	ES 2002-761678	20020916
US 20040204595	A1	20041014	US 2004-490186	20040319
US 7145024	B2	20061205		

PRIORITY APPLN. INFO.: US 2001-323692P P 20010920

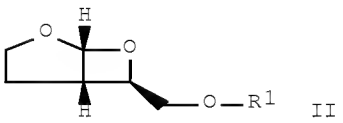
WO 2002-US29315 W 20020916

OTHER SOURCE(S): CASREACT 138:271663; MARPAT 138:271663

GI



I



II

AB The invention includes a method for preparing cyclic alcs. I (racemic or enantiomeric). The method involves a reduction, deprotection, and rearrangement, in non-aqueous telescoping conditions, of a bicyclic oxetane derivative II [R1 = C(R2)3, COR3, or Si(R3)3; R2 = (independently) H, alkyl, or aryl; R3 = (independently) alkyl or aryl]. The invention further provides a method of preparation of an intermediate useful in the synthesis of compds. that function as inhibitors of the aspartyl protease enzyme of human immunodeficiency virus (HIV). For instance, photochem. cycloaddn. of TBDMS-OCH2CHO with furan gave 98% yield of II [R1 = TBDMS, i.e., SiMe2Bu-tert]. The adduct underwent double-bond hydrogenation over water-wet 5% Pt/C in THF in the presence of K2CO3. This was followed (without isolation) by hydrolytic deprotection and rearrangement in THF solution in the presence of H2O and concentrated HCl, to give (±)-I in 82% yield (both steps). Racemic I was resolved by (1) O-acetylation with Ac2O, Na2CO3, and DMAP; (2) selective hydrolysis of the undesired enantiomer of the acetate using the lipase PS-800 in phosphate buffer at pH 6.8-7.2, giving the (3R,3aS,6aR)-acetate in >98% ee; and (3) hydrolysis using K2CO3 in MeOH at room temperature, giving (3R,3aS,6aR)-I. Other protecting groups for use in R1, namely PhCMe2, tert-Bu, and PhCH2, are exemplified.

IC ICM C07D493-04
ICS C07D307-00; C07D309-00; C07D305-00

CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 45

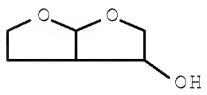
IT 109789-19-7P, Hexahydrofuro[2,3-b]furan-3-ol
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); IMF (Industrial manufacture); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(target intermediate; preparation of hexahydrofurofuranol racemate and enantiomer as intermediates for HIV aspartyl protease inhibitors)

IT 156928-09-5P, (3R,3aS,6aR)-Hexahydrofuro[2,3-b]furan-3-ol
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(target intermediate; preparation of hexahydrofurofuranol racemate and enantiomer as intermediates for HIV aspartyl protease inhibitors)

IT 162119-33-7P, (3α,3aβ,6aβ)-Hexahydrofuro[2,3-b]furan-3-ol
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(target intermediate; preparation of hexahydrofurofuranol racemate and enantiomer as intermediates for HIV aspartyl protease inhibitors)

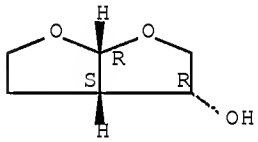
IT 109789-19-7P, Hexahydrofuro[2,3-b]furan-3-ol
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); IMF (Industrial manufacture); PUR (Purification or recovery); RCT (Reactant);

SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(target intermediate; preparation of hexahydrofurofuranol racemate and enantiomer as intermediates for HIV aspartyl protease inhibitors)
RN 109789-19-7 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro- (CA INDEX NAME)



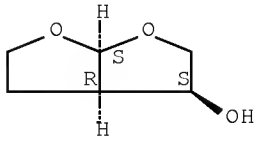
IT 156928-09-5P, (3R,3aS,6aR)-Hexahydrofuro[2,3-b]furan-3-ol
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(target intermediate; preparation of hexahydrofurofuranol racemate and enantiomer as intermediates for HIV aspartyl protease inhibitors)
RN 156928-09-5 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 162119-33-7P, (3α,3aβ,6aβ)-Hexahydrofuro[2,3-b]furan-3-ol
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(target intermediate; preparation of hexahydrofurofuranol racemate and enantiomer as intermediates for HIV aspartyl protease inhibitors)
RN 162119-33-7 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)-rel- (CA INDEX NAME)

Relative stereochemistry.



L78 ANSWER 16 OF 26 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:594851 ZCAPLUS Full-text
DOCUMENT NUMBER: 137:154919

TITLE: Preparation of 3-methylenehexahydrofuro[2,3-b]furan via photochemical cyclization of 3-halo-2-(2-propynyloxy)tetrahydrofurans.
INVENTOR(S): Davis, Roman; Lovelace, Thomas Clairborne
PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002060905	A2	20020808	WO 2001-US46116		20011022
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2002253800	A1	20020812	AU 2002-253800		20011022
WO 2002067239	A2	20020829	WO 2001-US51428		20011022
WO 2002067239	A3	20040108			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW					
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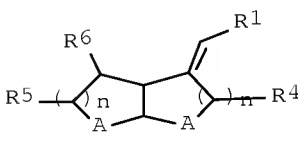
JP 2004519473	T	20040702	JP 2002-566479		20011022
US 20040026230	A1	20040212	US 2003-399809		20030423
PRIORITY APPLN. INFO.:			US 2000-242822P	P	20001024
			WO 2001-US46116	W	20011022
			WO 2001-US51428	W	20011022

OTHER SOURCE(S): CASREACT 137:154919; MARPAT 137:154919
GI



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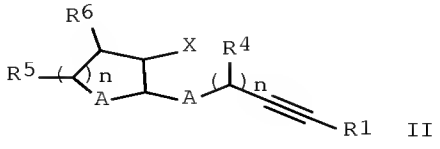


II

AB Title compds. (I; A = CH2, CHR10, CR10R11, O, NH, NR10, S; R10, R11 = H, alkyl, aryl; R1 = H, alkyl, aryl, heterocyclyl, alkylheterocyclyl; R4 = H, alkyl, aryl, alkylheterocyclyl, heterocyclyl; R5 = H, aryl, alkyl, alkylheterocyclyl, OR12, CH2OR12; R12 = alkyl, COR10; R6 = H, aryl, alkyl, alkylheterocyclyl, heterocyclyl, OR12, CH2OR12; n = 1-4), were prepared by exposure of alkynes (II; X = halo; other variables as above) to 200-400 nM light in the presence of NR7R8R9 (R7-R9 = H, aryl, alkyl, alkylheterocyclyl, heterocyclyl). Thus, 3-bromo-2-(2- propynyloxy)tetrahydrofuran in MeCN/Et3N was irradiated at 254 nM for 15-20 h to give 3-methylenehexahydrofuro[2,3-b]furan.

IC ICM C07D493-00

CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))

IT 109789-19-7P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of 3-methylenehexahydrofuro[2,3-b]furan via photochem. cyclization of 3-halo-2-(2-propynyloxy)tetrahydrofuran)

IT 156928-09-5P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of 3-methylenehexahydrofuro[2,3-b]furan via photochem. cyclization of 3-halo-2-(2-propynyloxy)tetrahydrofuran)

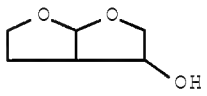
IT 109789-19-7P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of 3-methylenehexahydrofuro[2,3-b]furan via photochem. cyclization of 3-halo-2-(2-propynyloxy)tetrahydrofuran)

RN 109789-19-7 ZCAPLUS

CN Furo[2,3-b]furan-3-ol, hexahydro- (CA INDEX NAME)



IT 156928-09-5P

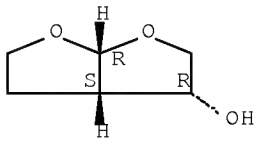
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of 3-methylenehexahydrofuro[2,3-b]furan via photochem. cyclization of 3-halo-2-(2-propynyloxy)tetrahydrofuran)

RN 156928-09-5 ZCAPLUS

CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L78 ANSWER 17 OF 26 ZCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:457100 ZCAPLUS Full-text

DOCUMENT NUMBER: 135:273092

TITLE: Stereoselective synthesis of optically active perhydrofuro[2,3-b]furan derivatives

AUTHOR(S): Uchiyama, M.; Hirai, M.; Nagata, M.; Katoh, R.; Ogawa, R.; Ohta, A.

CORPORATE SOURCE: School of Pharmacy, Tokyo University of Pharmacy and Life Science, Hachioji, Tokyo, 192-0392, Japan

SOURCE: Tetrahedron Letters (2001), 42(28), 4653-4656
CODEN: TELEAY; ISSN: 0040-4039

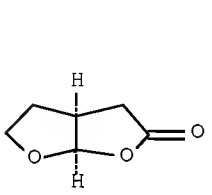
PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 135:273092

GI



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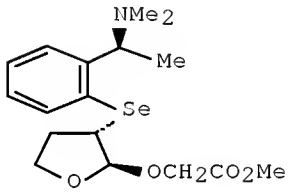
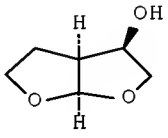


II



III

AB (1R,5S)-2,8-Dioxabicyclo[3.3.0]octan-3-one (I) and its derivs., important subunits in various biol. active natural products, were synthesized based on a new approach using the asym. oxyselenenylation of 2,3-dihydrofuran as the key step yielding II which was cyclized and resolved providing the major isomer III.

CC 30-20 (Terpenes and Terpenoids)

IT 156928-09-5P 252873-50-0P 362634-52-4P 362634-60-4P
362634-62-6P 362634-64-8P 362634-66-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(stereoselective preparation of optically active perhydrofuro[2,3-b]furan derivs.)

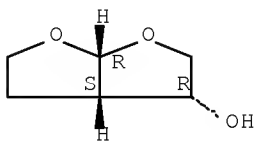
IT 152185-61-0P 156928-10-8P 362634-54-6P 362634-56-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(stereoselective preparation of optically active perhydrofuro[2,3-b]furan derivs.)

IT 156928-09-5P 252873-50-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(stereoselective preparation of optically active perhydrofuro[2,3-b]furan derivs.)

RN 156928-09-5 ZCAPLUS

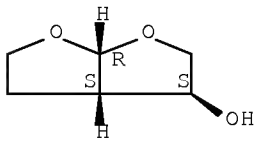
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



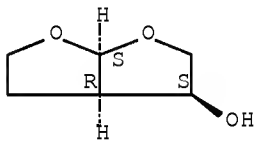
RN 252873-50-0 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3S,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 156928-10-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(stereoselective preparation of optically active perhydrofuro[2,3-b]furan derivs.)
RN 156928-10-8 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3S,3aR,6aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L78 ANSWER 18 OF 26 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:819523 ZCAPLUS Full-text
DOCUMENT NUMBER: 132:59135
TITLE: Fitness assay and associated methods, and applications to drug resistance and HIV protease inhibitors and other drugs with reduced resistance
INVENTOR(S): Erickson, John W.; Gulnik, Sergei V.
PATENT ASSIGNEE(S): United States of America, Represented by the Secretary, Department of Health and Human Services, USA
SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9967417	A2	19991229	WO 1999-US14119	19990623
WO 9967417	A3	20000928		

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            DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
            KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
            MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
            TR, TT, UA, UG, US, UZ, VN, YU, ZW
        RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
            ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
            CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     CA 2336160          A1    19991229    CA 1999-2336160        19990623
     AU 9948280          A     20000110    AU 1999-48280          19990623
     AU 771780           B2    20040401
     EP 1088098          A2    20010404    EP 1999-931861         19990623
        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, FI
     JP 2002518063       T     20020625    JP 2000-556057         19990623
     AU 2004200629       A1    20040311    AU 2004-200629         20040218
     AU 2004200629       B2    20070419
     US 20050158713      A1    20050721    US 2005-30632          20050106
     AU 2007203321       A1    20070809    AU 2007-203321         20070717
     US 20080085918      A1    20080410    US 2007-870931         20071011
PRIORITY APPLN. INFO.:                      US 1998-90393P      P  19980623
                                            AU 1999-48280       A3 19990623
                                            WO 1999-US14119     W  19990623
                                            US 2001-720276      A1 20010307
                                            AU 2004-200629      A3 20040218

OTHER SOURCE(S):        MARPAT 132:59135
GI   For diagram(s), see printed CA Issue.
AB   The invention provides an assay for determining the biochem. fitness of a
     biochem. species in a mutant replicating biol. entity relative to its
     predecessor.  The invention further provides a continuous fluorogenic assay
     for measuring the anti-HIV protease activity of protease inhibitor. The
     invention also provides a method of administering a therapeutic compound that
     reduces the chances of the emergence of drug resistance in therapy. The
     invention also provides a compound AXQN(R2)CH[(CH2)mR3]CH(R4)CH2N(R5)(WR 6) [A
     = Q1, Q2, Q3, Q4; R1, R2, R3, R5, R6 = H, (substituted and/or heteroatom-
     bearing) alkyl, alkenyl, alkynyl, or cyclic group; Y, Z = CH2, O, S, SO, SO2,
     amino, amides, carbamates, ureas, or thiocarbonyl derivs. thereof, optionally
     substituted with an alkyl, alkenyl, or alkynyl group; n = 1-5; X = bond,
     (substituted) methylene or ethylene, amino, O, S; Q = C(O), C(S), SO2; m = 0-
     6; R4 = OH, =O (keto), NH2, alkylamino, including esters, amides, and salts
     thereof; W = C(O), C(S), S(O), SO2; Optionally, R5 and R6, together with the
     NW bond comprise a macrocyclic ring], or a pharmaceutically acceptable salt, a
     prodrug, a composition, or an ester thereof.
IC   ICM  C12Q001-00
CC   1-1 (Pharmacology)
     Section cross-reference(s): 28, 63
IT   49676-93-9P   109789-17-5P   116949-62-3P   116949-67-8P   140867-26-1P
     156928-09-5P 156928-10-8P   159005-71-7P   162020-29-3P
     162119-33-7P   180902-29-8P   206361-96-8P   253265-96-2P
     253265-97-3P   253265-98-4P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP
     (Preparation); RACT (Reactant or reagent)
        (preparation and reaction; fitness assay and associated methods, and
        applications to drug resistance and HIV protease inhibitors and other
        drugs with reduced resistance)
IT   156928-09-5P 156928-10-8P 162119-33-7P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP
     (Preparation); RACT (Reactant or reagent)
        (preparation and reaction; fitness assay and associated methods, and
        applications to drug resistance and HIV protease inhibitors and other
```
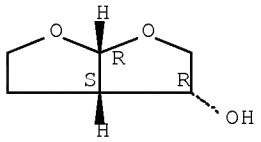
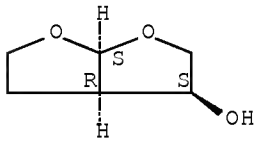

drugs with reduced resistance)
RN 156928-09-5 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



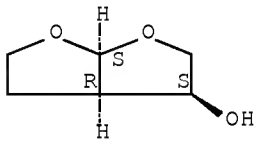
RN 156928-10-8 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3S,3aR,6aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 162119-33-7 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)-rel- (CA INDEX NAME)

Relative stereochemistry.



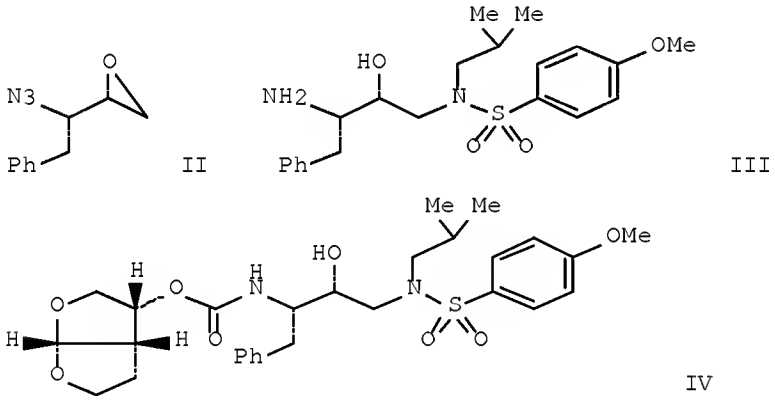
L78 ANSWER 19 OF 26 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:819380 ZCAPLUS Full-text
DOCUMENT NUMBER: 132:64254
TITLE: Multidrug-resistant retroviral protease inhibitors and associated methods
INVENTOR(S): Erickson, John W.; Gulnik, Sergei V.; Ghosh, Arun K.; Hussain, Khaja A.
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA; Board of Trustees of the University of Illinois
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9967254	A2	19991229	WO 1999-US14120	19990623
WO 9967254	A3	20000210		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9948281	A	20000110	AU 1999-48281	19990623
AU 2004200629	A1	20040311	AU 2004-200629	20040218
AU 2004200629	B2	20070419		
AU 2007203321	A1	20070809	AU 2007-203321	20070717

PRIORITY APPLN. INFO.:
US 1998-90393P P 19980623
AU 1999-48280 A3 19990623
WO 1999-US14120 W 19990623
AU 2004-200629 A3 20040218

OTHER SOURCE(S): MARPAT 132:64254

GI

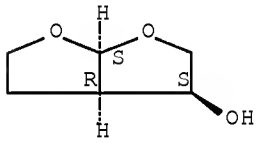


AB Nonpeptidic, retroviral protease-inhibiting compds. AZZ1NR2CH[(CH2)mR3]CHR4CH2NR5Z2R6 [I; A = heterocyclyl (structures specified); R2 = H, C1-6 alk(en)yl, C1-6 alkynyl; R3 = (un)substituted (hetero)cycloalkyl, (un)substituted (hetero)aryl; R4 = OH, O, NH2, NHMe; R5 = H, C1-6 alk(en)yl, etc.; R6 = (un)substituted (hetero)cycloalkyl, (un)substituted (hetero)aryl; R5R6 together with NZ2 bond can form a 12-18-membered ring containing ≥1 addnl. heteroatom; Z = bond, CHR10, O, S, NR10, etc.; R10 = (un)substituted alk(en)yl or alkynyl; Z1, Z2 = C(O), S(O), SO2; m = 0-6] or their pharmaceutically acceptable salts, prodrugs, or esters, were prepared Also provided are pharmaceutical compns. for, and therapeutic methods of treating a multidrug-resistant retroviral infection in a mammal. For example, azidoepoxybutane II (4-step preparation from butadiene monooxide and PhMgBr given) was subjected to ring cleavage/amination with Me2CHCH2NH2, the amine amidated with p-MeOC6H4SO2Cl and the azide function of the resulting amide

reduced by Pd-catalyzed hydrogenation to give aminosulfonamide III. Transamidation of the latter with (3R,3aS,6aR)-3-hydroxyhexahydrofuro[2,3-b]furyl succinimidyl carbonate (5-step preparation from dihydrofuran and propargyl alc. given) gave a title inhibitor IV which showed nanomolar and sub-nanomolar potency against several multidrug-resistant HIV-1.

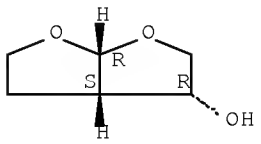
IC ICM C07D493-00
CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
IT 162119-33-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and enzymic resolution; preparation of multidrug-resistant retroviral
protease inhibitors and associated methods)
IT 156928-09-5P 156928-10-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and esterification with active carbonate; preparation of multidrug-resistant retroviral protease inhibitors and associated methods)
IT 162119-33-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and enzymic resolution; preparation of multidrug-resistant retroviral
protease inhibitors and associated methods)
RN 162119-33-7 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)-rel- (CA INDEX NAME)

Relative stereochemistry.



IT 156928-09-5P 156928-10-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and esterification with active carbonate; preparation of multidrug-resistant retroviral protease inhibitors and associated methods)
RN 156928-09-5 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

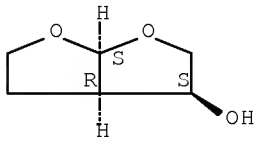
Absolute stereochemistry. Rotation (-).



RN 156928-10-8 ZCAPLUS

CN Furo[2,3-b]furan-3-ol, hexahydro-, (3S,3aR,6aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L78 ANSWER 20 OF 26 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:811207 ZCAPLUS Full-text
DOCUMENT NUMBER: 132:49801
TITLE: Preparation of 1-acylamino-3-(N-arylsulfonyl-N-alkoxyamino)-2-hydroxypropanes and related compounds as inhibitors of HIV aspartyl protease.
INVENTOR(S): Sherrill, Ronald George; Hale, Michael R.; Spaltenstein, Andrew; Furfine, Eric Steven; Andrews, Clarence Webster, III; Lowen, Gregory Thomas
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 344 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9965870	A2	19991223	WO 1999-US13744	19990617
WO 9965870	A3	20010315		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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AU 9945760	A	20000105	AU 1999-45760	19990617
AU 767728	B2	20031120		
EP 1086076	A1	20010328	EP 1999-928769	19990617
EP 1086076	B1	20041222		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9912169	A	20010410	BR 1999-12169	19990617
NZ 508855	A	20031031	NZ 1999-508855	19990617
AT 285396	T	20050115	AT 1999-928769	19990617
PT 1086076	T	20050531	PT 1999-928769	19990617
ES 2235492	T3	20050701	ES 1999-928769	19990617
AP 1717	A	20070228	AP 2000-2023	19990617
US 20020049201	A1	20020425	US 2000-731129	20001206
US 6613743	B2	20030902		
NO 2000006405	A	20010219	NO 2000-6405	20001215
MX 2000PA12637	A	20010405	MX 2000-PA12637	20001218

HK 1037605	A1	20051007	HK 2001-106764		20010925
US 20040097594	A1	20040520	US 2003-600937		20030620
NZ 528074	A	20041126	NZ 2003-528074		20030908
AU 2004200636	A1	20040311	AU 2004-200636		20040219
US 20060172936	A1	20060803	US 2005-212045		20050825
AU 2007234578	A1	20071213	AU 2007-234578		20071121
PRIORITY APPLN. INFO.:			US 1998-90094P	P	19980619
			WO 1999-US13744	W	19990617
			US 2000-731129	A3	20001206
			US 2003-600937	B3	20030620
			AU 2004-200636	A3	20040219

OTHER SOURCE(S): MARPAT 132:49801

AB ABxN(Gx)CHDCHOR7CH2ND'SO2E [A = H, (substituted) Ht, R1Ht, R1Ak; Ak = alkyl; Ht = cycloalkyl, cycloalkenyl, (substituted) aryl, heterocyclyl; R1 = CO, SO2, COCO, O2C, NR2CO, NR2SO2, etc.; B = null, NR2C(R3)2CO; x = 0, 1; R2 = H, (substituted) Ht, alkyl; R3 = H, (substituted) Ht, alkyl, alkenyl, cycloalkyl, cycloalkenyl; G = null, H, R7, alkyl; G may be bound to R7; D = (substituted) Q, alkyl, alkenyl; Q = (substituted) carbocyclyl, heterocyclyl; D' = OR10, N:R10, N(R10)R1R3; E = Ht, OHt, OR3, NR2R3, (substituted) alkyl, alkenyl, etc.; R7 = H, (CH2O)xY(ZM)(:X)Z(M)x, etc.; M = null, H, Li, Na, K, Mg, Ca, Ba, alkyl, alkenyl, etc.; X = O, S; Y = P, S; Z = O, S, N(R2)2, H], were prepared as inhibitors of HIV aspartyl protease (no data). Thus, 3-H2NC6H4SO2NHOCHMe2 (preparation given), tert-Bu N-(1S)-1-[(2S)-oxiran-2-yl]-2-phenylethylcarbamate, and phosphazene base P4 tert-Bu were stirred in 8 h in THF to give 95% tert-Bu N-(1S,2R)-3-[[(3-aminophenyl)sulfonyl](isopropoxy)amino]-1-benzyl-2- hydroxypropylcarbamate.

IC ICM C07C303-00

CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1, 27, 28, 34

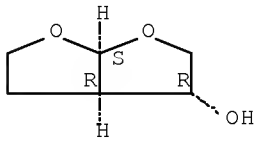
IT 3515-93-3P 21431-21-0P 23095-31-0P 25216-74-4P 51229-88-0P
51951-29-2P 54224-24-7P 57598-34-2P 69746-62-9P 84202-56-2P
87001-32-9P 113211-23-7P 132291-96-4P 134833-83-3P 162711-45-7P
169956-61-0P 169956-75-6P 169956-80-3P 252872-59-6P 252872-60-9P
252872-61-0P 252872-62-1P 252872-63-2P 252872-64-3P 252872-66-5P
252872-67-6P 252872-68-7P 252872-69-8P 252872-70-1P 252872-71-2P
252872-72-3P 252872-74-5P 252872-75-6P 252872-76-7P 252872-77-8P
252872-78-9P 252872-79-0P 252872-80-3P 252872-81-4P 252872-82-5P
252872-84-7P 252872-85-8P 252872-86-9P 252872-87-0P 252872-88-1P
252872-89-2P 252872-90-5P 252872-91-6P 252872-92-7P 252872-93-8P
252872-94-9P 252872-95-0P 252872-96-1P 252872-97-2P 252872-98-3P
252872-99-4P 252873-00-0P 252873-01-1P 252873-02-2P
252873-03-3P 252873-04-4P 252873-05-5P 252873-07-7P 252873-08-8P
252873-09-9P 252873-10-2P 252873-11-3P 252873-12-4P 252873-13-5P
252873-14-6P 252873-15-7P 252873-16-8P 252873-17-9P 252873-19-1P
252873-20-4P 252873-22-6P 252873-23-7P 252873-24-8P 252873-25-9P
252873-26-0P 252873-27-1P 252873-28-2P 252873-29-3P 252873-30-6P
252873-31-7P 252873-32-8P 252873-42-0P 252873-46-4P 252873-55-5P
252873-78-2P 252879-54-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 1-acylamino-3-(N-arylsulfonyl-N-alkoxyamino)-2-hydroxypropanes and related compds. as inhibitors of HIV aspartyl protease)

IT 252873-00-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 1-acylamino-3-(N-arylsulfonyl-N-alkoxyamino)-2-hydroxypropanes and related compds. as inhibitors of HIV aspartyl protease)

RN 252873-00-0 ZCAPLUS

CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aR,6aS)- (CA INDEX NAME)

Absolute stereochemistry.

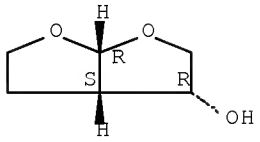


L78 ANSWER 21 OF 26 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:13236 ZCAPLUS Full-text
DOCUMENT NUMBER: 126:126512
ORIGINAL REFERENCE NO.: 126:24273a,24276a
TITLE: Evaluation of furofuran as a P2 ligand for symmetry-based HIV protease inhibitors
AUTHOR(S): Chen, Xiaoqi; Li, Lin; Kempf, Dale J.; Sham, Hing; Wideburg, Norman E.; Saldivar, Ayda; Vasavanonda, Sudthida; Marsh, Kennan C.; McDonald, Edith; Norbeck, Daniel W.
CORPORATE SOURCE: Pharm. Prod. Div., Abbott Lab., Abbott Park, IL, 60064, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1996), 6(23), 2847-2852
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The hexahydrofurofuranyloxy group was evaluated as a conformationally constrained P2 ligand for symmetry-based HIV protease inhibitors. A number of compds. showed nM level activity against HIV in MT4 cells and lower protein binding than the licensed protease inhibitor ritonavir. However, replacement of 5-thiazole of ritonavir with a furofuran caused a reduction of the bioavailability in vivo.

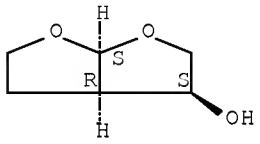
CC 1-5 (Pharmacology)
Section cross-reference(s): 7, 28
IT 156928-09-5P 156928-10-8P 186488-43-7P 186488-51-7P
186488-54-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction; furofuran as P2 ligand for symmetry-based HIV protease inhibitors)
IT 156928-09-5P 156928-10-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction; furofuran as P2 ligand for symmetry-based HIV protease inhibitors)
RN 156928-09-5 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



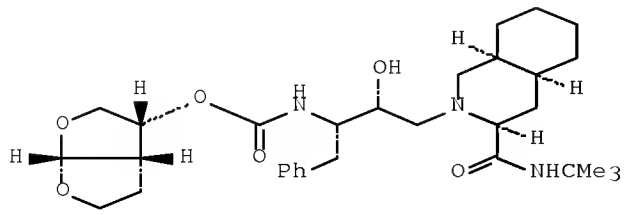
RN 156928-10-8 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3S,3aR,6aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L78 ANSWER 22 OF 26 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1996:452240 ZCAPLUS Full-text
DOCUMENT NUMBER: 125:221638
ORIGINAL REFERENCE NO.: 125:41425a,41428a
TITLE: Nonpeptidal P2 Ligands for HIV Protease Inhibitors: Structure-Based Design, Synthesis, and Biological Evaluation
AUTHOR(S): Ghosh, Arun K.; Kincaid, John F.; Walters, D. Eric; Chen, Yan; Chaudhuri, Narayan C.; Thompson, Wayne J.; Culberson, Chris; Fitzgerald, Paula M. D.; Lee, Hee Yoon; et al.
CORPORATE SOURCE: Department of Chemistry, University of Illinois, Chicago, IL, 60607, USA
SOURCE: Journal of Medicinal Chemistry (1996), 39(17), 3278-3290
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Design and synthesis of nonpeptidal bis-tetrahydrofuran ligands based upon the X-ray crystal structure of the HIV-1 protease-inhibitor Ro 31-8959 led to replacement of two amide bonds and a 10π-aromatic system of Ro 31-8959 class of HIV protease inhibitors. Detailed structure-activity studies have now established that the position of ring oxygens, ring size, and stereochem. are all crucial to potency. Of particular interest, I with (3S,3aS,6aS)-bis-Thf is the most potent inhibitor (IC50 value 1.8 ± 0.2 nM; CIC95 value 46 ± 4 nM) in this series. The X-ray structure of protein-inhibitor I has provided insight into the ligand-binding site interactions. As it turned out, both oxygens in the bis-Thf ligands are involved in hydrogen-bonding interactions with Asp 29 and Asp 30 NH present in the S2 subsite of HIV-1 protease. Stereoselective routes have been developed to obtain these novel ligands in optically pure form.

CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 10

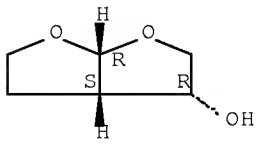
IT 156928-09-5P 156928-10-8P 167539-37-9P 181136-59-4P
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(design and preparation of nonpeptidal P2 ligands as HIV protease inhibitors)

IT 49826-08-6P 80997-80-4P 109789-17-5P 118616-28-7P 118867-18-8P
139402-85-0P 156879-12-8P 162020-29-3P 162119-33-7P
167539-34-6P 167817-21-2P 180902-23-2P 180902-24-3P 180902-25-4P
180902-26-5P 180902-27-6P 180902-28-7P 180902-29-8P 180902-30-1P
180902-31-2P 181136-57-2P 181136-58-3P 181136-60-7P 181136-61-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(design and preparation of nonpeptidal P2 ligands as HIV protease inhibitors)

IT 156928-09-5P 156928-10-8P
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(design and preparation of nonpeptidal P2 ligands as HIV protease inhibitors)

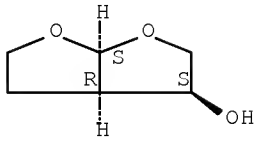
RN 156928-09-5 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



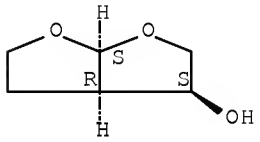
RN 156928-10-8 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3S,3aR,6aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 162119-33-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(design and preparation of nonpeptidal P2 ligands as HIV protease inhibitors)
RN 162119-33-7 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)-rel- (CA INDEX NAME)

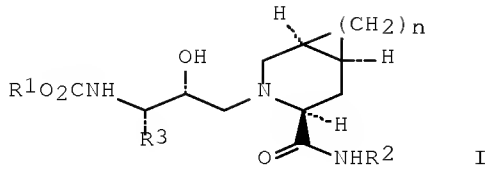
Relative stereochemistry.



L78 ANSWER 23 OF 26 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1995:784804 ZCAPLUS Full-text
DOCUMENT NUMBER: 123:198775
ORIGINAL REFERENCE NO.: 123:35485a,35488a
TITLE: Preparation of HIV protease inhibitors
INVENTOR(S): Ghosh, Arun K.; Thompson, Wayne J.; Mckee, Sean P.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9426749	A1	19941124	WO 1994-US5128	19940502
W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, HU, JP, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, TT, UA, UZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9468288	A	19941212	AU 1994-68288	19940502
PRIORITY APPLN. INFO.:			US 1993-61897 A	19930514
			WO 1994-US5128 W	19940502

OTHER SOURCE(S): MARPAT 123:198775
GI



I

AB The title compds. [I; R1 = (un)substituted bicyclic heterocyclic ring; R2 = (un)substituted C1-5 alkyl, (un)substituted carbocyclic; R3 = (un)substituted Ph, (un)substituted cycloalkyl; n = 3, 4] [e.g., (3S,4aS,7aS,2'R,3'S,3"R,3"aS,6"aR) N-tert-Bu octahydro-2-[2'-hydroxy-4'-phenyl-3'-(3"-hexahydrofuro[2,3-b]furanyloxycarbonylamino)butyl]-1H-pyrindene-3-carboxamide], useful in the inhibition of HIV protease (no data), the prevention or treatment of infection by HIV (no data), and the treatment of AIDS (no data), are prepared

IC ICM C07D493-04
ICS C07D405-12; A61K031-47; A61K031-35; A61K031-34

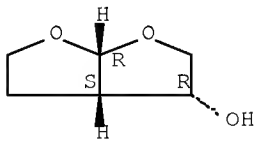
CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 34

IT 49676-93-9P 88335-90-4P 116949-62-3P 130432-72-3P 136465-81-1P
136465-90-2P 136522-17-3P 138499-08-8P 138499-09-9P 138499-10-2P
140867-26-1P 156879-12-8P 156928-09-5P 156928-10-8P
162776-59-2P 162776-60-5P 162776-61-6P 162776-62-7P 162870-69-1P
167539-29-9P 167539-30-2P 167539-31-3P 167539-32-4P 167539-33-5P
167539-34-6P 167539-35-7P 167539-36-8P 167539-37-9P 167539-38-0P
167817-17-6P 167817-18-7P 167817-19-8P 167817-20-1P 167817-21-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of HIV protease inhibitors)

IT 156928-09-5P 156928-10-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of HIV protease inhibitors)

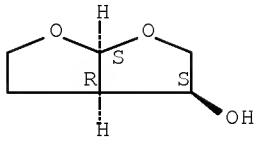
RN 156928-09-5 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

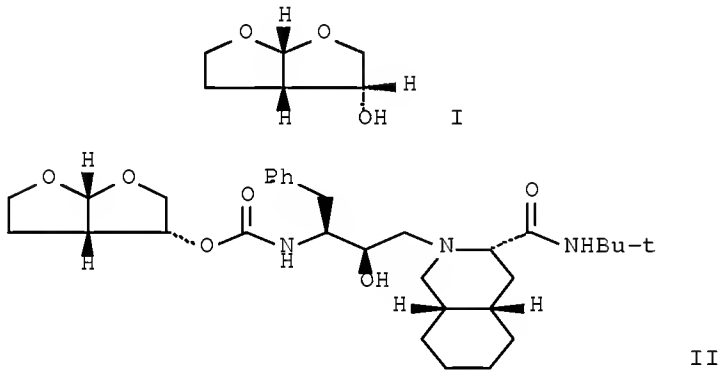


RN 156928-10-8 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3S,3aR,6aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L78 ANSWER 24 OF 26 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1995:357280 ZCAPLUS Full-text
DOCUMENT NUMBER: 122:239645
ORIGINAL REFERENCE NO.: 122:43801a,43804a
TITLE: Synthesis and optical resolution of high affinity P2-ligands for HIV-1 protease inhibitors
AUTHOR(S): Ghosh, Arun K.; Chen, Yan
CORPORATE SOURCE: Dept. Chem., Univ. Illinois at Chicago, Chicago, IL, 60607, USA
SOURCE: Tetrahedron Letters (1995), 36(4), 505-8
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 122:239645
GI



I

II

AB Racemic bis-tetrahydrofuran ligand, (±)-hexahydrofuro[2,3-b]furan-3-ol (I), was efficiently synthesized utilizing a cobaloxime-mediated radical cyclization as the key step. I was prepared as intermediate for [3-[3-[[(1,1-dimethylethyl)amino]carbonyl]octahydro-2(1H)-isoquinolinyl]-2- hydroxy-1-(phenylmethyl)propyl]carbamate hexahydrofuro[2,3-b]furan-3-yl ester II. Optical resolution of the racemic alc. with immobilized-Amano lipase, afforded optically pure ligands, i.e., [3R- (3α,3aβ,6aβ)]-hexahydrofuro[2,3-b]furan-3-ol and [3S-(3α,3aβ,6aβ)]-hexahydrofuro[2,3-b]furan-3-ol.

CC 28-18 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 27, 29

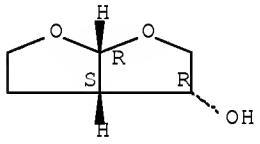
IT 109789-17-5P 156928-09-5P, [3R-(3α,3aβ,6aβ)]-Hexahydrofuro[2,3-b]furan-3-ol 156928-10-8P, [3S-(3α,3aβ,6aβ)]-Hexahydrofuro[2,3-b]furan-3-ol

162020-29-3P, [3S-(3α,3aβ,6aβ)]-Hexahydrofuro[2,3-b]furan-3-ol acetate 162119-33-7P 162119-35-9P 180902-29-8P 186488-43-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of hexahydrofuro[2,3-b]furan-3-yl [[(aminocarbonyl)isoquinoliny l]hydroxypropyl]carbamate)

IT 156928-09-5P, [3R-(3α,3aβ,6aβ)]-Hexahydrofuro[2,3-b]furan-3-ol 156928-10-8P, [3S-(3α,3aβ,6aβ)]-Hexahydrofuro[2,3-b]furan-3-ol 162119-33-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of hexahydrofuro[2,3-b]furan-3-yl [[(aminocarbonyl)isoquinoliny l]hydroxypropyl]carbamate)

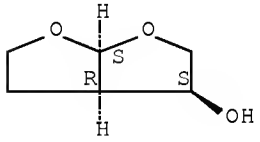
RN 156928-09-5 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



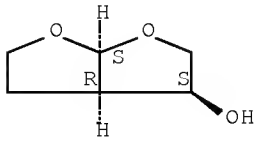
RN 156928-10-8 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3S,3aR,6aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

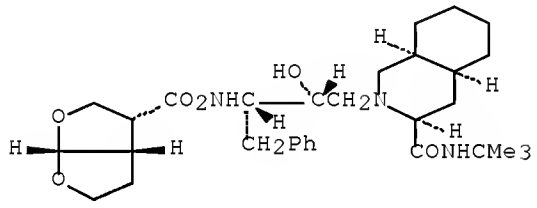


RN 162119-33-7 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)-rel- (CA INDEX NAME)

Relative stereochemistry.



L78 ANSWER 25 OF 26 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1994:621038 ZCAPLUS Full-text
DOCUMENT NUMBER: 121:221038
ORIGINAL REFERENCE NO.: 121:39957a,39960a
TITLE: Structure-Based Design of HIV-1 Protease Inhibitors: Replacement of Two Amides and a 10π-Aromatic System by a Fused Bis-tetrahydrofuran
AUTHOR(S): Ghosh, Arun K.; Thompson, Wayne J.; Fitzgerald, Paula M. D.; Culberson, J. Chris; Axel, Melinda G.; McKee, Sean P.; Huff, Joel R.; Anderson, Paul S.
CORPORATE SOURCE: Department of Medicinal Chemistry, Merck Research Laboratories, West Point, PA, 19486, USA
SOURCE: Journal of Medicinal Chemistry (1994), 37(16), 2506-8
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

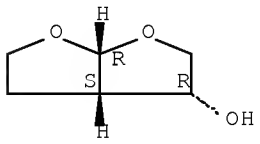


I

AB The structure-based design of a conformationally constrained fused bistetrahydrofuran effectively replaces 2 amide bonds and a 10π-aromatic system of the present clin. candidate, Ro 31-8959. The inhibitor (I) (IC50 = 1.8 nM,; CIC95 = 46 nM) thus obtained, showed comparable in vitro antiviral activities to inhibitors in the hydroxyethylamine class with both P2 and P3 ligands. To obtain information regarding the ligand binding site interactions, a single crystal of the inhibitor I complexed with HIV-1 protease was generated, and the 3-dimensional structure was determined by x-ray diffraction to 2.10 Å resolution Interestingly, the oxygen-1 and oxygen-6 of the bis-tetrahydrofuran ligand are within hydrogen bonding distance to the Asp 29 NH and Asp 30 NH present in the S2 binding domain of the HIV-1 protease. The design and synthesis of such a high affinity ligand led to improved aqueous solubility and reduction in mol. weight due to exclusion of the P3 ligand.

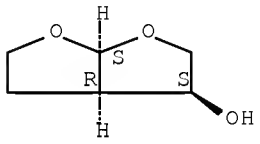
CC 1-3 (Pharmacology)
Section cross-reference(s): 28
IT 156928-09-5P 156928-10-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with dipyridyl carbonate)
IT 156928-09-5P 156928-10-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with dipyridyl carbonate)
RN 156928-09-5 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

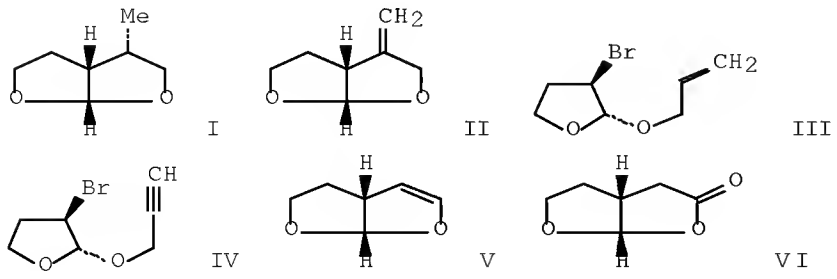


RN 156928-10-8 ZCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3S,3aR,6aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L78 ANSWER 26 OF 26 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1987:477655 ZCAPLUS Full-text
DOCUMENT NUMBER: 107:77655
ORIGINAL REFERENCE NO.: 107:12777a,12780a
TITLE: A new route to perhydro- and tetrahydrofuro[2,3-b]furans via radical cyclization
AUTHOR(S): Pezechk, M.; Brunetiere, A. P.; Lallemand, J. Y.
CORPORATE SOURCE: Lab. Synthese Org., Ec. Polytech., Palaiseau, Fr.
SOURCE: Tetrahedron Letters (1986), 27(32), 3715-18
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 107:77655
GI



AB Perhydrofuro[2,3-b]furans I and II were prepared in almost quant. yields by the radical cyclization of unsatd. bromo acetals III and IV, resp., in the presence of Bu3SuH. II was transformed into tetrahydro derivative V in 4 steps. The radical annulation of ICH2CO2SnBu3 to 2,3-dihydrofuran gave perhydro[2,3-b]furanone VI.

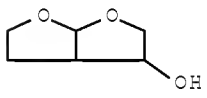
CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))

IT 109789-19-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and tosylation of)

IT 109789-19-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and tosylation of)

RN 109789-19-7 ZCAPLUS

CN Furo[2,3-b]furan-3-ol, hexahydro- (CA INDEX NAME)



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=> d his full

     (FILE 'HOME' ENTERED AT 09:55:53 ON 03 JUN 2008)

     FILE 'ZCAPLUS' ENTERED AT 09:56:29 ON 03 JUN 2008
                E US2006-599497 /APPS
L1            2 SEA ABB=ON  PLU=ON  US2006-599497 /AP
                D SCA
L2            1 SEA ABB=ON  PLU=ON  L1 AND PREP?/TI
                SEL RN

     FILE 'REGISTRY' ENTERED AT 09:57:27 ON 03 JUN 2008
L3           17 SEA ABB=ON  PLU=ON  (104321-62-2/BI OR 124-41-4/BI OR 156928-09
                -5/BI OR 22323-80-4/BI OR 501921-30-8/BI OR 6674-22-2/BI OR
                67-63-0/BI OR 75-52-5/BI OR 75-65-0/BI OR 75-75-2/BI OR
                75-85-4/BI OR 80-70-6/BI OR 865-34-9/BI OR 866594-60-7/BI OR
                866594-61-8/BI OR 867-13-0/BI OR 94697-68-4/BI)
                D SCA
L*** DEL2228299 S OC4/ESS (S) OC4/ESS
L4         84397 SEA ABB=ON  PLU=ON  2 OC4/ESS
L5             4 SEA ABB=ON  PLU=ON  L3 AND L4
                D SCA
L6          1642 SEA ABB=ON  PLU=ON  C6H10O3/MF
L7            22 SEA ABB=ON  PLU=ON  L6 AND L4
                D SCA
L8             1 SEA ABB=ON  PLU=ON  L5 AND L7
                D SCA
L9            21 SEA ABB=ON  PLU=ON  L7 NOT L8
                D SCA
L10           20 SEA ABB=ON  PLU=ON  "FURO(2,3-B)FURAN-3-OL, HEXAHYDRO-"?/CN
L11            1 SEA ABB=ON  PLU=ON  L8 AND L10
L12            7 SEA ABB=ON  PLU=ON  L7 AND L10
                D SCA
L13           13 SEA ABB=ON  PLU=ON  L10 NOT L12
                D SCA

     FILE 'ZCAPLUS' ENTERED AT 10:06:28 ON 03 JUN 2008
L14           43 SEA ABB=ON  PLU=ON  L12

     FILE 'REGISTRY' ENTERED AT 10:06:45 ON 03 JUN 2008
                SEL RN L12
L15            0 SEA ABB=ON  PLU=ON  (109789-19-7/CRN OR 156928-09-5/CRN OR
                156928-10-8/CRN OR 162119-33-7/CRN OR 252873-00-0/CRN OR
                252873-50-0/CRN OR 869565-59-3/CRN)
L16            3 SEA ABB=ON  PLU=ON  L5 NOT L12
                D SCA
L17         1147 SEA ABB=ON  PLU=ON  C7H10O4/MF
L18           32 SEA ABB=ON  PLU=ON  L17 AND L4
L19           29 SEA ABB=ON  PLU=ON  L18 NOT L16
                D SCA

     FILE 'ZCAPLUS' ENTERED AT 10:11:28 ON 03 JUN 2008
L20            5 SEA ABB=ON  PLU=ON  L16
L21            3 SEA ABB=ON  PLU=ON  L14 AND L20
                D SCA
                SEL RN

     FILE 'REGISTRY' ENTERED AT 10:15:14 ON 03 JUN 2008
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L22          32 SEA ABB=ON  PLU=ON  (104321-62-2/BI OR 156928-09-5/BI OR
                22323-80-4/BI OR 867-13-0/BI OR 94697-68-4/BI OR 108-59-8/BI
                OR 204390-79-4/BI OR 501921-30-8/BI OR 866594-60-7/BI OR
                124-41-4/BI OR 144114-21-6/BI OR 252873-00-0/BI OR 501921-23-9/
                BI OR 501921-24-0/BI OR 501921-25-1/BI OR 501921-26-2/BI OR
                501921-27-3/BI OR 501921-28-4/BI OR 501921-29-5/BI OR 501921-31
                -9/BI OR 501921-32-0/BI OR 6674-22-2/BI OR 67-63-0/BI OR
                75-52-5/BI OR 75-65-0/BI OR 75-75-2/BI OR 75-85-4/BI OR
                80-70-6/BI OR 865-34-9/BI OR 866594-61-8/BI OR 874290-09-2/BI
                OR 874290-10-5/BI)
L23     1933411 SEA ABB=ON  PLU=ON  ?NITRO?/CNS
L24           4 SEA ABB=ON  PLU=ON  L22 AND L23
                D SCA

     FILE 'ZCAPLUS' ENTERED AT 10:15:59 ON 03 JUN 2008
L25           2 SEA ABB=ON  PLU=ON  L24 AND L21

     FILE 'REGISTRY' ENTERED AT 10:16:37 ON 03 JUN 2008
                D SCA L12
                D SCA L16
L*** DEL      0 S ?"FURO(3,4-B)FURAN"?/CNS
L26         835 SEA ABB=ON  PLU=ON  "FURO(3,4-B)FURAN"?/CN
L27         727 SEA ABB=ON  PLU=ON  "FURO(2,3-B)FURAN"?/CN

     FILE 'ZCAPLUS' ENTERED AT 10:20:48 ON 03 JUN 2008
L28         146 SEA ABB=ON  PLU=ON  L26 (L) RACT/RL
L29         287 SEA ABB=ON  PLU=ON  L27 (L) PREP/RL
L30           4 SEA ABB=ON  PLU=ON  L28 AND L29
                SEL RN
                SEL HIT RN
L31           1 SEA ABB=ON  PLU=ON  L30 NOT L21
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 10:21:43 ON 03 JUN 2008
L32          12 SEA ABB=ON  PLU=ON  (109789-17-5/BI OR 150330-64-6/BI OR
                156879-12-8/BI OR 156879-13-9/BI OR 156928-09-5/BI OR 156928-10
                -8/BI OR 156928-12-0/BI OR 162020-29-3/BI OR 162119-33-7/BI OR
                180902-24-3/BI OR 180902-27-6/BI OR 180902-28-7/BI)
                D SCA

     FILE 'ZCAPLUS' ENTERED AT 10:24:01 ON 03 JUN 2008
L33             TRA PLU=ON  L14 1- RN :    3468 TERMS

     FILE 'REGISTRY' ENTERED AT 10:24:03 ON 03 JUN 2008
L34        3468 SEA ABB=ON  PLU=ON  L33
L35         102 SEA ABB=ON  PLU=ON  L34 AND L23
L36          50 SEA ABB=ON  PLU=ON  L35 AND ?NITROPHENYL?/CNS
L37          52 SEA ABB=ON  PLU=ON  L35 NOT L36
                D SCA
L38           4 SEA ABB=ON  PLU=ON  L37 AND ?NITROMETHYL?/CNS

     FILE 'ZCAPLUS' ENTERED AT 10:29:03 ON 03 JUN 2008
L39           2 SEA ABB=ON  PLU=ON  L38 AND L14
                D SCA

     FILE 'CASREACT' ENTERED AT 10:30:15 ON 03 JUN 2008
L40          18 SEA ABB=ON  PLU=ON  L12
L41           3 SEA ABB=ON  PLU=ON  L16
L42           1 SEA ABB=ON  PLU=ON  L40 (L) L41
                D SCA
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     FILE 'REGISTRY' ENTERED AT 10:31:19 ON 03 JUN 2008

     FILE 'CASREACT' ENTERED AT 10:31:36 ON 03 JUN 2008
L43             TRA PLU=ON  L40 1- RX :     431 TERMS

     FILE 'REGISTRY' ENTERED AT 10:32:42 ON 03 JUN 2008
L44           431 SEA ABB=ON  PLU=ON  L43/RN
L45            16 SEA ABB=ON  PLU=ON  L44 AND L23
                  D SCA
L46             1 SEA ABB=ON  PLU=ON  L45 AND L24
                  D RN

     FILE 'CASREACT' ENTERED AT 10:34:10 ON 03 JUN 2008
L47          4646 SEA ABB=ON  PLU=ON  75-52-5
L48             1 SEA ABB=ON  PLU=ON  L40 (L) L47
L49             1 SEA ABB=ON  PLU=ON  L42 AND L48
                  D SCA

     FILE 'REGISTRY' ENTERED AT 10:38:28 ON 03 JUN 2008

     FILE 'ZCAPLUS' ENTERED AT 10:38:32 ON 03 JUN 2008
                  D STAT QUE L21
                  D STAT QUE L25
                  D STAT QUE L39
L50            52 SEA ABB=ON  PLU=ON  QUAEDFLIEG P?/AU
L51            33 SEA ABB=ON  PLU=ON  KESTELEYN B?/AU
L52            15 SEA ABB=ON  PLU=ON  VIJN R?/AU
L53             3 SEA ABB=ON  PLU=ON  LIEBREGTS C?/AU
L54            46 SEA ABB=ON  PLU=ON  KOOISTRA J?/AU
L55            10 SEA ABB=ON  PLU=ON  LOMMEN F?/AU
L56             3 SEA ABB=ON  PLU=ON  L50 AND (L51 OR L52 OR L53 OR L54 OR L55)
L57             2 SEA ABB=ON  PLU=ON  L51 AND (L52 OR L53 OR L54 OR L55)
L58             3 SEA ABB=ON  PLU=ON  L52 AND (L53 OR L54 OR L55)
L59             2 SEA ABB=ON  PLU=ON  L53 AND (L54 OR L55)
L60             1 SEA ABB=ON  PLU=ON  L54 AND L55
L61             3 SEA ABB=ON  PLU=ON  (L56 OR L57 OR L58 OR L59 OR L60)
L62         63018 SEA ABB=ON  PLU=ON  L4
L63             4 SEA ABB=ON  PLU=ON  (L50 OR L51 OR L52 OR L53 OR L54 OR L55)
                  AND L62
                  D SCA
L64             0 SEA ABB=ON  PLU=ON  (L42 OR L48) AND (L50 OR L51 OR L52 OR L53
                  OR L54 OR L55)
L65            43 SEA ABB=ON  PLU=ON  L12
L66             5 SEA ABB=ON  PLU=ON  L16
L67             4 SEA ABB=ON  PLU=ON  (L65 OR L66) AND (L50 OR L51 OR L52 OR L53
                  OR L54 OR L55)
                  SEL AN

     FILE 'CASREACT' ENTERED AT 10:44:45 ON 03 JUN 2008
L68             3 SEA ABB=ON  PLU=ON  ("138:238003"/AN OR "143:387012"/AN OR
                  "144:170908"/AN OR "148:379603"/AN OR "2003:221694"/AN OR
                  "2005:1103784"/AN OR "2005:1257726"/AN OR "2008:381168"/AN)
                  D SCA
L69             2 SEA ABB=ON  PLU=ON  L68 NOT L42
L70             2 SEA ABB=ON  PLU=ON  L69 AND (L40 OR L41)
                  D SCA
L71             3 SEA ABB=ON  PLU=ON  L68 AND (L40 OR L41 OR L42)

     FILE 'REGISTRY' ENTERED AT 10:47:45 ON 03 JUN 2008
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     FILE 'ZCAPLUS' ENTERED AT 10:47:54 ON 03 JUN 2008
                D STAT QUE L61
                D STAT QUE L63
L72             5 SEA ABB=ON  PLU=ON  L61 OR L63

     FILE 'CASREACT' ENTERED AT 10:48:15 ON 03 JUN 2008
                D STAT QUE L71

     FILE 'ZCAPLUS' ENTERED AT 10:49:00 ON 03 JUN 2008
                D IBIB ABS HITIND HITSTR L72 TOT

     FILE 'CASREACT' ENTERED AT 10:49:09 ON 03 JUN 2008
                D IBIB ABS HIT L71 TOT

     FILE 'REGISTRY' ENTERED AT 10:50:48 ON 03 JUN 2008

     FILE 'ZCAPLUS' ENTERED AT 10:50:51 ON 03 JUN 2008
                D STAT QUE L21
                D STAT QUE L25
                D STAT QUE L39
L73             1 SEA ABB=ON  PLU=ON  (L21 OR L25 OR L39) NOT L72

     FILE 'CASREACT' ENTERED AT 10:51:27 ON 03 JUN 2008
                D STAT QUE L42
                D STAT QUE L48
L74             0 SEA ABB=ON  PLU=ON  (L42 OR L48) NOT L71

     FILE 'ZCAPLUS' ENTERED AT 10:51:52 ON 03 JUN 2008
L75             1 DUP REM L73 L74 (0 DUPLICATES REMOVED)
                       ANSWER '1' FROM FILE ZCAPLUS
                D IBIB ABS HITIND HITSTR L75 1
L76            30 SEA ABB=ON  PLU=ON  L12 (L) PREP/RL
L77            26 SEA ABB=ON  PLU=ON  L76 NOT L72

     FILE 'REGISTRY' ENTERED AT 10:54:13 ON 03 JUN 2008

     FILE 'ZCAPLUS' ENTERED AT 10:54:16 ON 03 JUN 2008
                D STAT QUE L76
L78            26 SEA ABB=ON  PLU=ON  L76 NOT (L72 OR L73)
                D IBIB ABS HITIND HITSTR L78 1-26


     FILE HOME

     FILE ZCAPLUS

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     FILE COVERS 1907 - 3 Jun 2008  VOL 148 ISS 23
     FILE LAST UPDATED: 2 Jun 2008  (20080602/ED)
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DICTIONARY FILE UPDATES: 2 JUN 2008 HIGHEST RN 1024742-83-3

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http://www.cas.org/support/stngen/stndoc/properties.html

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FILE CONTENT:1840 - 31 May 2008 VOL 148 ISS 23

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This file contains CAS Registry Numbers for easy and accurate substance identification.

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